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PRIMARY CEREBRAL HYDATID DISEASE*

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THIS subject has always been of interest to Australian surgeons—although few meet with many cases. Through the courtesy of my neurosurgical colleagues, I submit for consideration the story of ten Australian cases of this disease. Some of the cases have been recorded before, but now they are compared with others so that a more complete picture of the protean clinical manifestations is obtained. It is often valuable to review one's opinions in the light of fuller information and I find that a careful study of these ten cases has caused me to modify opinions that I have previously expressed (Dew, 1934). Perhaps, too, this short review may stimulate others to record their experiences with hydatid disease in this situation.

General

The characteristics of the disease in this situation are well known. It occurs much more commonly in young subjects, having developed as a primary cyst from a hexacanth embryo carried to the brain by the blood stream. Owing to the comparatively large size of the carotid arteries in a child a fairly high proportion of the embryos must be carried to the brain where the usual result of encystment is the formation of a single univesicular cyst. A cyst in this site grows rapidly because of the soft non-resistant nature of the cerebral tissue and its ample blood supply. Pressure effects on the brain usually manifest themselves within the first decade so that the child develops signs of raised intracranial pressure and eventually undergoes an operation or dies: thus adult life is rarely reached with an intact primary cyst.

It is obvious that many cases, although owing to the lack of full autopsy records the exact proportion is not known, may harbour a cyst in the liver or lung so that one should always suspect the association of a cerebral cyst with one in these regions.

Pathology

Primary cysts are usually single so that any case showing multiple cysts should be at once suspected to be an example of secondary echinococcosis derived by the spread of scolices from an intracardiac rupture of a left-sided cardiac cyst. The typical cyst is univesicular and it was once thought that daughter cyst formation was very rare and that it was probably associated with some injury to the cranium, a not uncommon happening in childhood. The cyst, as a rule, commences its growth in the cerebral substance, quietly enlarging and compressing the brain substance or the ventricular system until it produces pressure effects which are manifested clinically in the usual way. A cyst may expand or erode the bones of the skull, must reach the surface of the brain if it has a diameter of approximately 10 cm., or involve the lateral ventricles; rupture into either of these directions may produce dramatic and serious symptoms. There is, as a rule, although this is not so universal as once thought, very little reaction in the glial tissue

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so that typically the adventitious capsule is ill-defined or practically absent. When the cyst impinges on the surface of the cortex the arachnoid and dura may become locally adherent. Sometimes the cerebral tissue seems to be simply pushed aside and the pia mater may still remain covering over the convolutions on which pressure is being exerted. Some very big cysts have been recorded and it is a matter for surprise how the intracranial contents adapt themselves with so few pathological changes and so few clinical effects. This is mainly due to the yielding nature of the growing skull which, as in cases of hydrocephalus, expands to make room for the cyst and to the surprising compensatory powers of young nervous tissue. The cysts are usually fertile, degenerations so commonly seen in other situations being relatively rare while calcification of the adventitia was previously recorded as being unknown. Some degree of deformity of the ventricular system must occur in every situation with varying degrees of block and increased intraventricular pressure.

CLINICAL ASPECTS

The average age of presenting patients is about 10 years, a figure which is found in all parts of the world. Owing to slow growth of the cyst the disease is strangely latent and as far as the cerebrum is concerned this is equalled by no other lesion. The progress of symptoms is slow and a period of one to two years from the onset may elapse before they become serious. The symptomatology is essentially that of a simple space-occupying non-filtrating lesion of the hemisphere, the exact syndrome depending on the site of the lesion.

General symptoms of increased intracranial pressure predominate and except in "hydatid" countries the exact nature of the lesion may remain totally unsuspected. In some cases, of course, focal symptoms may give rise to classical localizing signs. The pressure of the cerebrospinal fluid is almost invariably raised, sometimes to a high figure, but it is rare for there to be any significant alteration of its protein or chloride content. The skull, as well as showing the effects of raised intracranial pressure may also show localized bulging or even perforation, an indication of the length of time the lesion may have been present. In addition to this change in the skull there may be some localized tenderness, or a "cracked pot" sound on percussion. The Casoni intradermal test is very unreliable and this is not surprising as it depends upon the sensitization of the patient's tissues with specific hydatid antigen and this is not a marked feature in simple univesicular cysts. A positive finding is, of course, of real diagnostic value. The complement deviation test is of practically no value in these cases. The diagnosis depends on a full and accurate examination of the nervous system and the use of the various ancillary modes of investigation that have been developed as an aid to diagnosis and localization. If these modes of investigation are properly used diagnostic errors in the future should be largely eliminated.

The above is a very general statement of the accepted views concerning these cysts. The following series of ten cases from Australian sources, for the full records of which I am indebted to various colleagues, have been chosen because they illustrate some of the vagaries of cerebral hydatid cysts. They also show some of the errors that may occur in diagnosis and some of the problems associated with their management.

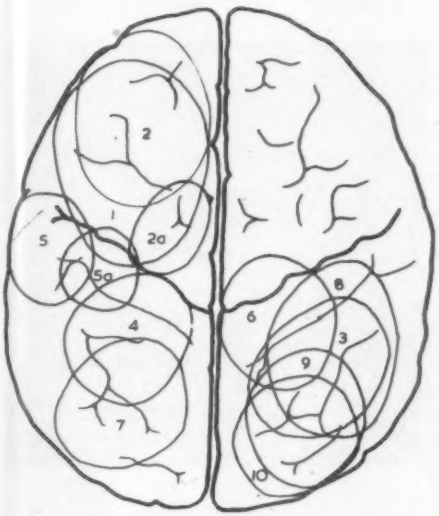
Case 1. Left frontal univesicular cyst (Phillips, 1948)

K.H., a male, age 11 years, was admitted with a history of slow mental deterioration, intermittent headaches and failing vision.

On examination he had a bilateral papilloedema, some degree of proptosis greater on the left than on the right side, a C.S.F. pressure of 420 mm., but no localizing neurological signs. The Casoni test was positive.

X-ray of the skull showed general enlargement, separation of the anterior sutures and enlarged sella turcica, some increase in the convolutional markings and thinning and erosion of the frontal bones. The original diagnosis of internal hydrocephalus seemed confirmed. A ventriculogram showed both lateral ventricles to be dilated, but it was found impossible to move the air from right to left. As a result, a tentative diagnosis of block of the foramen of Monro by a colloid cyst or other tumour of the third ventricle was made. An exploratory operation through the frontal horn of the right lateral ventricle was undertaken, the foramen of Monro was exposed

and examined but no tumour in the area was found. The patient stood this exploration well and was discharged temporarily, but was readmitted in a few months with all his symptoms increased in severity. A second ventriculogram was taken and this showed distortion of the left lateral ventricle, shift of the left lateral ventricle to the right with distention of both sides of the system. A diagnosis of a large left frontal tumour was made.



SITE OF CYSTS

FIG. I. This shows in schematic form the situations of the cysts under discussion.

A large bone flap over the left frontal area was turned down, a univesicular hydatid cyst of the lobe was aspirated, treated with formalin, carefully evacuated and closed without drainage. Fig. II shows the large cavity (12 x 15 cm.) with some air in it after operation. The patient made an interrupted recovery and is apparently cured.

Comment. This case is of interest because of:

(1) The simulation of ordinary internal hydrocephalus by high intracranial pressure, distended ventricles, distorted sella turcica and the changes in the skull bones. The significance of the local frontal bone erosion and the positive Casoni test obviously should have been appreciated.

(2) The extraordinary latency as regards symptoms of a very large left frontal cyst, the largest in the series, which had caused gross distortion of the ventricular system.

(3) The erroneous diagnosis of a colloid cyst or tumour blocking the foramen of Monro; this was due to an incorrect interpretation of the first ventriculogram.

(4) The fact that the patient survived the risk of a gross cerebral dislocation from left to right when the right frontal craniotomy and exploration were carried out: the patient was rather lucky in this regard.

(5) That the correct operation was ultimately carried out over the site of a very large cyst with apparent cure of the condition.

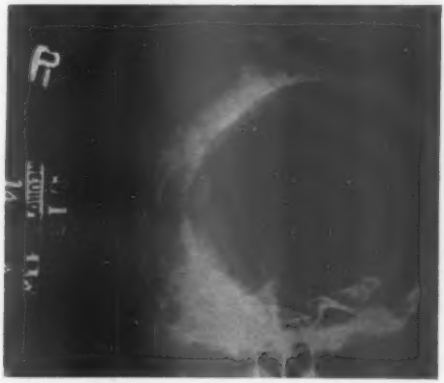


FIG. II. Post-operative radiograph showing large cyst in Case 1.

Case 2. A large partly calcified cyst of the left frontal lobe (Miller and Fleming, 1948)

I.M., a male, aged 8 years, was admitted with a history of having had a severe convulsion at the age of 4, several fits since then and increasing headaches for one year. Eight weeks before admission paresis of the right leg, arm and face developed.

On examination he had an extensor plantar reflex and obvious signs of paresis. He exhibited bilateral papilloedema and some contraction of the visual fields. A Casoni intradermal test was negative. X-ray of the skull showed the outline of a large calcareous cyst of the left frontal lobe (Fig. III).

The diagnosis of hydatid cyst was made and a large frontal osteoplastic flap was turned down. The arachnoid and dura were found to be adherent over a large bulging cyst. This was opened and was found to contain many daughter cysts, fluid and some debris. The adventitia was thick and irregularly calcified, feeling rather like a thick eggshell. Posteriorly there was a small opening through which a number of daughter cysts were removed. Removal of the rigid non-collapsible calcareous wall was debated, but it was finally filled with Ringer's

solution and closed without drainage. The patient's symptoms largely disappeared and he was discharged from hospital much improved, but he returned a month later with a recrudescence of his fits, followed by an attack of unconsciousness. Aspiration through a burr hole obtained 75 cc. of slightly blood stained fluid from the cavity and penicillin solution 1:1000 was introduced into this. X-ray was then taken after injection of 20 cc. of air into the cavity and showed what appeared to be a multiloculated cyst (Fig. IV).

FIG. III. Case 2, showing calcareous change in hydatid cyst of the left frontal lobe.

As the patient's condition deteriorated and the symptoms increased in severity the area was explored through a larger osteoplastic flap two months after the first operation. The old cavity was found to be filled with slightly turbid fluid and daughter cysts, while behind this was another large collection of daughter cysts apparently in connection with the small track noticed posteriorly at the first operation. The whole of the calcified cyst wall and the posterior collection with its adventitia was then carefully dissected out — a formidable performance which exposed nearly all the floor of the anterior fossa of the skull.

The surrounding brain tissue was compressed and atrophic while the ependyma of the lateral ventricle was exposed medially. In spite of local and systemic penicillin and the classical treatment of meningitis the patient died from meningitis some twenty days later. Autopsy revealed this particularly marked in the base with gross ventricular obstruction. No hydatid cysts were found in the brain or elsewhere in the body.

Comment. This case presents:

(1) The unusual feature of a well-developed calcareous adventitia in a large cyst in a young subject. This is very rare and the first of which I have had record.

(2) The presence of numerous daughter cysts in such a young subject is also important. It would seem that the onset of the first serious convulsion four years before admission probably coincided with the spread of the scolices from the original cyst posteriorly, and that the condition can probably be regarded as a variety of localized secondary echinococcosis.

FIG. IV. Case 2. Cystogram taken after the first operation showing communicating cysts of the left frontal lobe.

(3) The fatal meningitis was an unfortunate complication following the trauma of formidable surgical procedures. It is, of course, very easy to be wise after the event, but it still remains hard to decide what should have been the perfect procedure in this case. It rather emphasizes the importance of widely uncapping the cyst wall in order to visualize the whole of the inside of the cavity and to make sure that no hydatid material is left behind.

(4) The problem of what to do in the case of a thick or calcified adventitia within the brain is a very difficult one just as it is sometimes in other situations. Provided asepsis is perfect and provided all hydatid debris is completely removed and using a cover of systemic antibiotics it would seem that the best thing to do in the case of an otherwise uncomplicated cyst would be to completely clean the cavity, fill with Ringer's solution and close without drainage. In this

particular case it is possible that a wide excision of the whole lesion at the first operation would have revealed its complicated nature and would have got rid of all hydatid material. Admittedly this would have been a very formidable undertaking and it may be that even this would not have led to a satisfactory cure.

Case 3. A large cyst of right parietal lobe

D.B., a female, aged 23, was admitted to hospital complaining of very severe headaches and vomiting for a period of twelve months. She had had attacks suggesting the dreamy states of uncinate type and some attacks of unconsciousness.

On examination she was rather fat, had marked hirsuties but was relatively alert. She showed some tremor of the left hand, bilateral papilloedema of 2 diopters and a left homonymous quadrantopsia affecting the upper quadrant (Fig. V). The Casoni test was negative. X-ray of the skull showed an enlarged sella turcica and some thumb markings of the inner table.

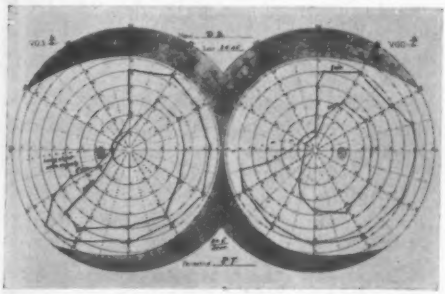


FIG. V. Case 3. Fields of vision showing left homonymous quadrantopsia.

She was for a time regarded as a possible tumour of the pituitary although the age and fields of vision negatived this. A ventricular needle was introduced through a right burr hole and struck a cyst at a depth of 3 cm., the fluid being under high pressure and containing 780 mm. per cent. of sodium chloride, but no hydatid elements. It was thought to be a hydatid cyst and some air was introduced. X-ray then revealed a very large cyst of the right parietal lobe extending as far forward as the Rolandic fissure. At operation a right parietal osteoplastic flap revealed at a depth of 1½ cm. a large simple hydatid cyst. This was partly emptied by a needle and 10 cc. of 10 per cent. formalin was injected and allowed to act for 5ve minutes. This was then evacuated, the cavity completely cleaned out and filled with Ringer's solution and closed without drainage. The patient made an uneventful recovery.

Comment.

(1) This case illustrates the well-known error of regarding sellar enlargement or erosion as being due to a pituitary lesion, whereas in many cases it is due to long standing intracranial pressure. The gross general symptoms, the localizing signs of left tremor and the fields of vision findings should have at once excluded this.

(2) It emphasizes the importance of investigating the fields of vision by means of a Bjerrum screen. In this case the defect in the fields was typical of a lesion involving the right lower parietal region, this being also somewhat suggested by the peculiar almost uncinate seizures.

(3) The use of a ventricular needle was unnecessary and in any case it should have been used on the left side, that is the side opposite to which the lesion was known to exist. It is doubtful whether air studies were required at all because localization should have been made without them. The risk of indiscriminate puncture of a cyst is not very great, but there must always arise the chance of the spread of scolices into the adventitial space and just as intrabronchial rupture may be precipitated by exploratory puncture of a pulmonary cyst so here there is a risk of precipitating rupture into the lateral ventricle. The successful result in this case in that recrudescence of symptoms has not occurred after a period of 8 years does not excuse what must, I think, be regarded as an unnecessary procedure.

Case 4. Left post-parietal multivesicular cyst

R.S., a male, aged 7 years, was admitted with a history of headaches which had been present for some four months and with paresis of the right side including the face. This occurred during an epidemic of anterior poliomyelitis and for a time this disease was actually suspected. However, he showed an extensor plantar reflex, some loss of sensation on the right side, obvious muscular weakness and astereognosis in the right hand. There was bilateral papilloedema of 1½ diopters and an interesting homonymous crescentic defect in his fields of vision. He also showed a marked "cracked pot" sound on percussion of the skull. The Casoni test was negative; no lumbar puncture or air studies were carried out because of the increased intracranial pressure. Simple X-ray of the skull showed separation of sutures, thinning of the skull and a large bulge over the left parietal and frontal regions.

A diagnosis of hydatid disease was made and operation through a large posterior parietal flap revealed localized pulging of the dura in the angle between the Rolandic fissure and the sagittal sinus extending well into the parietal lobe. Opening of the dura showed some adhesions to the arachnoid, but

they were easily separated and a curved arachnoid flap was then turned down revealing that the cyst contained numerous daughter cysts (Fig. VI).

FIG. VI. Case 4. Operative view showing daughter cysts present after opening arachnoid.

There was a very small amount of fluid present, this being quite clear. Without rupturing any of the cysts they were rolled out of the incision and the still intact mother cyst was seen deeper in the cavity. This had a small hole in it, but had not completely collapsed and it contained clear fluid. This fluid was aspirated carefully to reduce the total volume and to allow delivery of the intact partially collapsed mother cyst. The cavity was repeatedly washed out with Ringer's solution, followed by a weak 2 per cent. formalin which was allowed to act for two minutes to counteract any scolical contamination and then fully washed out. There was practically no adventitia except on the outer aspects and in the depths; the compressed convolutions of the upper part of the insula could be seen covered with what appeared to be normal pia mater. The cyst was large, being 10 cm. in its largest diameter and extended from near the sagittal sinus to the Sylvian fissure and under part of the motor cortex. It was filled with Ringer's solution and the cranium was closed without drainage. Recovery was uneventful.

Comment.

(1) This case is a good example of an ideal surgical procedure; no unnecessary air studies and an accurate diagnosis made on the classical findings of motor weakness, sensory interference and localized bone bulging. Approach through a large flap which exposed the whole of the cyst wall fully enabled it to be uncapped properly and all the parasitic tissue removed intact without contamination. It also enabled a complete toilet and treatment of the whole cavity under vision.

(2) The interest lay in the presence of multiple daughter cysts of fair size, up to 2 cm. in diameter, which had probably developed from scolices shed through the small hole in the laminated membrane of the original mother cyst. This is obviously a case of localized secondary echinococcosis in which extension had been almost entirely outwards. Adhesions between the arachnoid and dura around the edge of the bulging cyst precluded any extension beyond. The mother cyst contained a few brood capsules and degenerating scolices but they could not be proved viable by warming and it is almost certain that they were inert. There was no definite history of a fall or an episode at a previous time which would correlate with the age of these cysts, probably about two years. In the case of a young child, of course, it is very hard to exclude mild degrees of injury to the head.

(3) The almost complete absence of adventitia except at the outer aspects of the cyst where protective adhesions had been formed.

(4) The negative Casoni reaction was rather interesting because in a case of this nature one would rather expect it to be positive.

Case 5. Left parieto-temporal cysts (Hailes, 1935)

R.M., a female, aged 44, was admitted with a history of severe headaches for six months, a little difficulty with her speech, right facial paresis and weakness of the right arm and leg. Reflexes on the right were somewhat exaggerated but the plantar reflex was flexor in type. Lack of co-operation made examination of the visual fields unsatisfactory, but there was blurring of the optic discs although it could not be called a true papilloedema. X-ray of the skull showed nothing abnormal and no air studies were considered necessary. The diagnosis of a tumour involving the left motor cortex was made and operation through a large left osteoplastic flap was carried out. A subcortical swelling in the middle temporal region was uncapped and found to be a simple hydatid cyst 7.5 cm. in diameter, there being a very thin adventitia. The fluid, which contained a large number of scolices, was evacuated by puncture and the intact laminated membrane coaxed out. The wound was closed without drainage and the patient was discharged greatly improved. Eight months later weakness of the right hand, leg and face reappeared and she complained of some left frontal headache. The fundi were normal and the fields of vision by ordinary perimeter showed no defect. The old osteoplastic flap was re-elevated and another hydatid cyst without any true adventitia was found bulging on the surface a little cranial to the site of the first one. This cyst was 6.5 cm. in

diameter, perhaps a little smaller than the first one, was cleanly removed and the cavity washed out with weak formalin. The patient made an uninterrupted recovery and is still alive after eighteen years.

Comment.

These two cysts were typical simple cysts and undoubtedly of the same age and stage of development, although the question as to whether they were primary or secondary was at once raised. In spite of the infrequency of primary infestation in an adult of this age I believe that the most rational explanation is that they were both primary cysts. Although I do not know of any proved case of multiple primary cerebral cysts there is no reason why it should not happen here as in other sites. It is hard to believe that two secondary cysts of this size could have arisen from the left side of the heart particularly as there was nothing in the history suggestive of this, nor was there any evidence of primary cysts being discovered then or later. I do not believe that it was a cyst derived from the sowing of a scolex at the original operation because no secondary cyst derived from a scolex could reach this size within eight months. Although my late surgical colleague would not probably have agreed I believe that the second cyst was present adjacent to the first from the beginning and that the decompressive effect of the removal of the first cyst allowed and indeed encouraged the second cyst to make its way towards the original operative site. This phenomenon is not unknown in the liver and most surgeons have noticed the appearance of a large second cyst near the site from which a cyst had been removed at a previous operation. I think the phenomenon is probably identical in both cases.

Case 6. A right parietal cyst

R.G., a male, aged 3 years and 4 months, was admitted with a history that he was noticed dragging his left foot. Then a limp due to paresis developed and his left arm became weak. These symptoms had developed during two months. There were no complaints of headaches or vomiting and there were no abnormal findings on examining his central nervous system. He had an early bilateral papilloedema, but his fields of vision were not investigated because of his early age. X-ray of the skull showed no abnormality. Ventricular puncture on the right side was attempted; fluid under pressure was encountered and at first this was thought to be a large ventricle and seemed to confirm the suspicion that he had a certrally placed tumour causing internal hydrocephalus. Some air was run in and a second X-ray showed a cyst high up in the parietal region containing air with a fold across it suggesting a hydatid cyst with collapsed laminated membrane. Operation through a parietal flap demonstrated the cyst which was evacuated, formalinized and treated without drainage. The patient made an uneventful recovery.

Comment. The interest of this case lies in:

(1) The extreme youth of the patient—the youngest in the series and the youngest of which I have record.

The cyst was not so large as many are. It produced no bony deformity but owing to its site it produced focal symptoms of paresis early in its history before signs of high intracranial pressure had developed.

(2) These symptoms and signs in themselves should have been sufficient to lead to a correct diagnosis and if it was thought necessary to perform a ventriculogram it should have been done on the left side.

(3) The appearance in the cystogram of a fold of membrane across the cyst gave an appearance very suggestive of what in pulmonary cysts has been called the sign of the *Calotte* by some South American observers. This has been noticed on several occasions in cystograms of cerebral cysts.

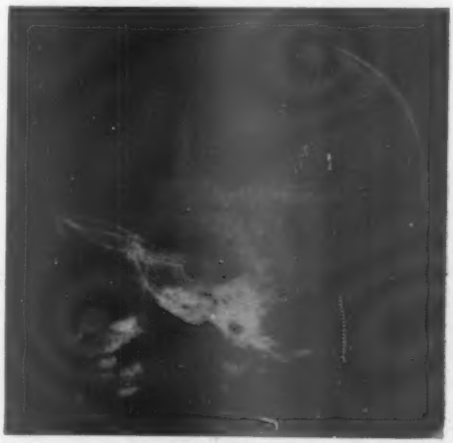


FIG. VII. Case 6. Cystogram showing fold of membrane across cyst cavity.

Case 7. Left occipito-parietal cyst

D.P., a male, aged 13, was admitted with severe headaches and vomiting over a period of eight months, together with some loss of visual acuity.

On examination he exhibited no neurological abnormality. His poor vision and bilateral papilloedema of 2 diopters and his severe headaches precluded an accurate examination of his visual fields. The Casoni test was negative. A skull X-ray showed some increase of convolutional markings, slight separation of the coronal sutures, but no bony abnormality. Ventricular estimation through occipital burr holes was carried out. The right needle struck the lateral ventricle at a depth of 4.5 cm., the fluid pressure being within normal limits. The left needle struck fluid at a depth of 2 cm., the fluid being at a much higher pressure than the right. The asymmetry of the ventricles showed the lesion was not centrally placed so air was allowed to flow into both sides in order to obtain a ventriculogram. It was suspected that the left-sided collection might be a hydatid cyst although no hooklets or scolices were found in the fluid. The X-ray showed a large air containing cyst at least 10 cm. in diameter in the left occipital lobe, with a fold of laminated membrane stretching across it (Fig. VIII).

FIG. VIII. Case 7. Cystogram showing large cyst of the occipital lobe with fold of laminated membrane across the cavity.

Stretched across the cyst cavity was a shadow due to a fold of collapsed laminated membrane rather similar to the preceding case. Operation through a posteriorly placed flap revealed a cortical bulging and at a depth of just under 2 cm., a large hydatid cyst was opened. Fluid and cyst membrane were evacuated by suction but because of the presence of the thin wall of the lateral ventricle in the depth, the use of formalin was regarded as inadvisable so irrigation and suction only were used. The cavity was filled with Ringer's solution and the cranium closed without drainage.

The patient made an uneventful recovery, had no fits whatever in the years following — in fact, he became a skilled air pilot in World War 2.

Comment.

(1) This is a typical case of a simple hydatid cyst in the occipital area except that the fields of vision should have shown homonymous hemianopia. In this case as with many young subjects it may prove difficult to obtain significant and accurate findings from this examination. It may call for great patience and tact and one must always remember that these patients tire easily and may give inaccurate responses.

(2) The introduction of a ventricular needle into the cyst made the diagnosis relatively easy particularly as the pressure was high—pressure in many simple hydatid cysts may reach 300 mm. of mercury. Although the fluid contained no hydatid elements at that examination it had a very high sodium chloride content. It emphasizes, I think, the need for the most careful examination of any fluid obtained by exploratory brain puncture, as surprises so often occur.

Case 8. Cyst of right occipito-parietal region

I.T., a male, aged 10 years, was admitted with a history of very severe headaches for over a year, these were associated with vomiting. He had had a severe fit a little over one year before admission, and some tremor of the left hand had been quietly developing. He had had several other convulsions during the year and these were always followed by severe headache.

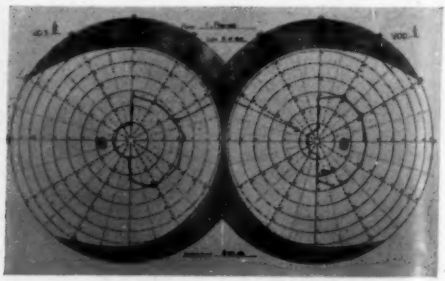


FIG. IX. Case 8. Fields of vision showing left homonymous hemianopia—complete quantitative estimation was not done because of the patient's fatigue, but the findings were clear cut and adequate for diagnostic purposes.

On examination he had no abnormal reflex phenomenon, but showed bilateral early papilloedema. Fields of vision showed left homonymous hemianopia (Fig. IX).

The Casoni test was negative. Plain X-ray of the skull showed evidence of increased intracranial pressure. On attempting ventricular puncture through an occipital burr hole the right hand needle

struck slightly yellow fluid at fairly high pressure at a depth of 1 cm. Air was introduced and a large cyst containing air was demonstrated by X-ray. Operation through a posterior flap revealed a very large hydatid cyst containing numerous daughter cysts which was opened through a relatively small opening. After the aspiration of nearly 12 oz. of slightly yellow fluid the folded laminated membrane of the mother cyst and numerous daughter cysts were removed from a cyst which extended well forward to the fissure of Rolando. No formalin was used as it was thought that in the presence of numerous daughter cysts it had not much value and because of the large size of the cavity it was felt that the ventricular ependyma might be endangered. The cavity was evacuated by pump and irrigation until it was thought to be quite clean and then closed without drainage. The patient did very well and was discharged free of symptoms and with improved visual fields. He returned, however, after eight months with recrudescence of all his symptoms, rapidly became comatose and died before any further intervention was possible. At autopsy a large number of daughter cysts, some of them up to 2 cm. in diameter, were found in the region of the old cavity extending from the parietal lobe into the temporal area. These escaped freely when the brain was removed from the calvarium. There were no cysts elsewhere in the body.

Comment.

(1) Puncture of a cyst of this size during ventriculography is almost inevitable although it probably did not do any real harm. Involvement of the optic radiation was also to be expected. The yellowish tinged fluid at first led to a suspicion of cystic astrocytoma before the radiograph was inspected. It is, of course, quite possible to find fluid in a hydatid cyst containing daughter cysts which is not perfectly clear and this possibility should always be remembered. The fluid also contained numerous scolices, though whether these were viable or not was not determined. It is most likely that they were not really viable as they were lying free.

(2) There seems little doubt that the recrudescence of symptoms was due to residual daughter cysts, either in the anterior part of the lesion or in a loculus in the temporal region. The case is, in this way, slightly similar to Case 5. It is notoriously difficult to be sure that all daughter cysts are removed; this is particularly so when the adventitia is weak, irregular or hardly existent. It might be suggested that the cysts present at autopsy were derived from scolices spread at the first operation and that therefore the use of formalin might have precluded their development. It is, I think, much more likely that the large daughter cysts, which were 2 cm. in diameter, were really original cysts overlooked at the first operation. It is quite impossible for a scolex to develop into a secondary cyst of this size within eight months. Information that we have from cases of secondary hydatid cysts developed in the brain from scolices derived from a simple cardiac cyst show that it takes about three years for them to reach a diameter of 2.5 cm.

(3) Looking back on this case it is difficult to decide whether the patient could have been saved. It is possible that a larger opening with better visualization of the inside of the cavity, guarding against contamination and making sure of the evacuation of all elements might have prevented recrudescence.

Case 9. Right occipital cyst

T.B., a male, aged 7, was admitted with a history of intense headaches and daily vomiting of cerebral type. He had few neurological signs except a high C.S.F. pressure. On examination he showed bilateral papilloedema and left homohymous hemianopia. The skull gave a "cracked pot" sound on percussion and a plain X-ray showed some separation of the sutures. X-ray also revealed a pulmonary hydatid cyst which had previously caused some hemoptysis. As might have been expected the Casoni reaction was positive. Electroencephalography showed delta dysrhythmia over the right post-parietal area and the diagnosis of a space occupying lesion in the parietal hemisphere was confirmed. Burr holes were made over the occipital region and a needle on the right side passed into a cyst at a depth of 2 cm., 40 cc. of clear fluid under pressure suggesting hydatid cyst was removed and 2 cc. of thoraplast introduced. X-rays then showed a large cystic cavity in the occipital lobe extending forward in the parietal area and the diagnosis of hydatid cyst was made (Fig. X). Operation a few days later showed a cyst near the surface; it was uncapped, evacuated and cleaned out without any contamination. It extended to the midline and obliterated a large part of the occipital lobe. The adventitia was very well developed over most of the sphere and the anterior two-thirds were dissected out to facilitate collapse of the cavity. During the operation the hydatid cyst of the lung ruptured into the bronchus and the anaesthetist had to remove a large piece of membrane from the larynx with a bronchoscope during the operation. The patient made a full recovery and about four months later was re-admitted and the lung cyst was dealt with by open surgical operation.

Comment.

(1) This case was localized by straight neurological examination and the diagnosis of hydatid cyst was at once suspected because of the age and the presence of a hydatid cyst in the lung; a lucky coincidence really. The

first exploration and the injection of thoraplast gave a perfect picture although it was really unnecessary.

(2) Operative procedure was straight forward and was only of particular interest because of the accidental intrabronchial rupture of the pulmonary cyst which except for the presence of mind of the anaesthetist might have been fatal.

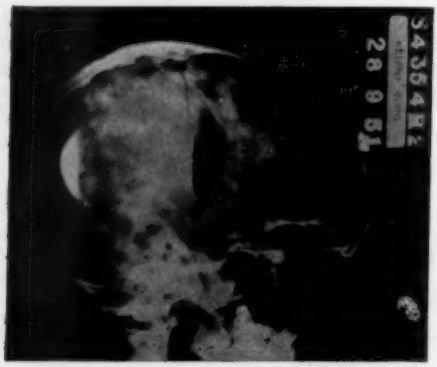


FIG. X. Case. 9. Cystogram (thorotrast and air) of occipital cyst.

Case 10. Right occipital cyst

B.H., a female, aged 17, was admitted with a history that she had had attacks of vertigo, some attacks of blackness, with a subjective sensation of objects moving around her from left to right. She then developed severe headaches and supra-orbital pain and had some attacks of diplopia. These symptoms had been present for twelve months.

On examination she showed no abnormal neurological signs except a left homonymous hemianopia (Fig. XI).

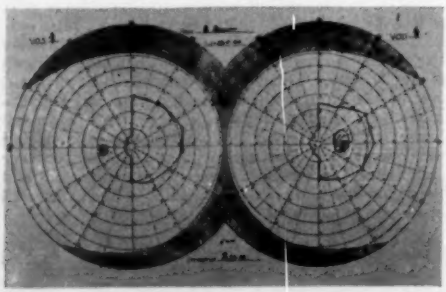


FIG. XI. Case 10. Fields of vision showing left homonymous hemianopia.

The plain X-ray showed increased convolutional markings and erosion of the sella turcica. A ventricular needle was passed through a right-sided burr hole and a cyst was struck very close to the cortex, 65 cc. of clear fluid were removed and replaced with air. X-ray then showed a large cavity in the right occipital region and the diagnosis of hydatid cyst was made. Operation was undertaken and when the original burr hole was exposed it was found that a piece of laminated membrane from the cyst was being extruded from the cranium. The burr hole was enlarged somewhat, the dura incised more freely and after a better exposure more fluid was evacuated and the whole of the laminated membrane was coaxed out through this small opening. The cavity was then formalinized, cleaned, irrigated and finally closed without drainage. Recovery was uneventful and four months later the visual fields were largely restored.

Comment.

This is another example of the value of fields of vision investigation in these posteriorly placed cysts and also of the discovery of a cyst during attempted ventriculogram. The mode of removal is probably unique, but one can hadly regard it as an ideal surgical procedure because of the difficulty of being sure of evacuation and sterilization of the cyst.

CONCLUSIONS

Apart from the fact that this group of cases illustrates the protean nature of hydatid disease and that one can always learn from a study of this disease there are other lessons to be learnt. They may be stated as follows:

1. While single simple cysts are the rule in the brain and while the adventitious capsule is often poorly developed, more than one cyst may occur and the adventitia may be not only tough and fairly thick but even calcified.

2. Daughter cyst formation even in very young subjects is not so very uncommon, and although this is possibly due to mild injury, which may be more or less indirect, there is in the three cases here recorded no proved relationship between the two events.

3. The extreme latency of the disease particularly in the so-called silent areas of the cerebrum, the frontal and occipital regions, must be emphasized but in "hydatid" countries any large lesion of the cerebrum in youth should be suspect.

4. The importance of the accurate estimation of the fields of vision is unquestioned as any cyst of the hemispheres

behind the frontal area which is producing symptoms must be large enough to affect the optic radiation. In this way it is possible to determine the side of the lesion and if macular sparing can be demonstrated place it in the occipital region.

5. If air studies are deemed advisable, although owing to the increasing emphasis being laid on purely neurological methods of diagnosis, they are not needed so frequently, it is advisable to introduce air into the ventricle opposite to the side of the lesion. The cases illustrate how often attempted ventricular punctures has found the cyst. Although this in itself leads to an accurate diagnosis it is always inadvisable as it must introduce unnecessary risks.

6. Thinning or deformity of the skull remains an important diagnostic finding and should always be carefully looked for in cerebral lesions in children. These may be associated with a typical "cracked pot" sound on percussion.

7. The Casoni intradermal test is unreliable although a positive one is of diagnostic value.

8. Operation exposure should be through a large osteoplastic flap after an accurate localization. Most cysts reach a diameter of about 10 cm. before producing symptoms and they must impinge somewhere on the arachnoid in nearly every case. It is of great help in the operation if the cyst can be dealt with quickly without fear of scolical contamination.

9. At operation the cyst should be uncapped, partially evacuated and injected with 5 per cent. formalin which should be allowed to act for two to three minutes and then sucked and washed out carefully. In those cases in which daughter cysts are present this has little value until the completion of the evacuation when it should be used quickly to fix any scolices in the depths. In these cases complete visualization of the cavity is essential if recurrences are to be avoided. Care must be taken in those cases in which the wall of the lateral ventricle can be seen in the wall of the cavity not to use formalin except through the medium of small swabs under vision.

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THE GEORGE ADLINGTON SYME ORATION

ON MAKING INAUGURAL ORATIONS

By Sir James Learmonth, K.C.V.O., C.B.E., Ch.M., F.R.C.S.E.

Regius Professor of Clinical Surgery and Professor of Surgery, University of Edinburgh

TO be asked to give the George Adlington Syme Oration to the Royal Australasian College of Surgeons is a high distinction, for which I thank the President and Council formally on behalf of the Edinburgh Medical School and on my own behalf. For you to have made the delivery of this address the first engagement of my visit as Sims Professor was a gesture at once courteous, friendly—and possibly confiding. That you should have arranged that I give my oration as an Honorary Fellow of this College is an honour and a delicate compliment which I shall always treasure.

I believe that the practice of attaching to an oration the name of a great figure in the medical history of a country is wholly admirable. There are three possible stipulations which might be made in the invitation to deliver such an address. The first, and perhaps the most natural, is a request that the address shall extol the man whose name it bears. You will acquit me, I hope, of any presumption if I agree with the Royal Australasian College of Surgeons because they have not imposed this condition. Sir George Syme's professional attainments, and the esteem in which he was held both in Australia and in Britain, are so secure that any eulogy of mine would be superfluous; and did he not "see Shelley plain" when he worked with Lord Lister, the Master, seventy years ago? The second stipulation may be that the orator is enjoined to justify his selection for so considerable an office by a description of his own work; the eschewing of this condition — no doubt reached in the private deliberations of your President and Council — adds to the responsibility which I feel today. The third possible stipulation is not a condition at all—it leaves the Syme Orator free to choose his own topic: possibly with the hope, felt but not officially expressed, that it would be one of which Syme, with his unlimited interests in life at every point, would not have disapproved. Lest my argument preclude my saying it later, may I say now, Sir, that I am well aware that an unconditional invitation is in the best tradition of academic ideals.

Some twenty-three years ago, the Hunterian Orator of the Royal College of Surgeons of England chose to make his address, not on John Hunter himself, but on the general topic of "The Commemoration of Great Men": I know that I cannot hope to reach the standard set by Wilfred Trotter, the most intellectually gifted of British surgeons of this century; but I too have chosen to speak on a general problem; the problem (or problems) involved in the making of inaugural addresses.

Clearly the most important of these is the choice of a topic. A number of perplexities confront a surgeon who has been honoured by an invitation to address a distinguished company of mixed composition. If his audience were to be composed solely of his colleagues, his natural choice of subject would be one in which he had a professional interest; and—this choice made—he might attempt to satisfy the cultural requirements of so important an occasion by approaching his theme from every possible angle, so complying with the elder Kocher's dictum that "one can obtain spiritual satisfaction from a profession only by making oneself master of every aspect of one branch of it." Indeed he might possibly justify the choice of a surgical topic for an oration to a mixed audience, by reflecting that an education is not liberal unless it includes a certain acquaintance with scientific matters, and that the best liberal educations familiarize the student with scientific methods of thought. Surgery has long been recognized to be an art: and no one would deny that modern surgery is also a science. As a matter of fact, for many centuries the union of art and science in the

practice of medicine and surgery has been recognized as both necessary and highly respectable. In his advice to the laity on the choosing of a doctor, the erudite Bacon took pains to emphasize the desirability of combining both approaches: "Physicians are some of them so pleasing and conformable to the humour of the patient as they press not the true cure of the disease; and some others are so regular in proceeding according to art for the disease as they respect not sufficiently the condition of the patient. Take one of middle temper; or, if it may not be found in one man, combine two of either sort; and forget not to call as well the best acquainted with your body as the best reputed for his faculty."

Yet he who would attempt to expound either or both aspects of a surgical topic—however simply—to a mixed audience would find himself confronted with two difficulties which would merit the adjective peculiar.

The first of these was summed up by that great physician Sir William Osler: "In all matters relating to disease credulity remains a permanent fact, uninfluenced by civilization or education." Thus any assembly which includes laymen may be expected to contain a proportion of people—I suspect astonishingly high—who are willing to use scientific standards in scrutinizing matters pertaining to the physical sciences, but who resolutely refuse to apply these standards in questions relating to their own health, or—much less pardonably—in questions relating to the health of others. They will accept the aeroplane and wireless communication: they will not accept inoculation and the knife. From time to time every medical man encounters this attitude, which is the expression of a persisting uneasy belief in the supernatural, and well he knows how unpredictable its appearance is; in despair I have watched the slow death from cancer of a great classical scholar who was convinced to the end that he was being cured by a decoction of the flowers of violets. To those similarly credulous a surgical topic might appear to be merely fictional.

The other primary difficulty is that of communication. Only the simplest of surgical topics can be dealt with adequately without the use of words either unfamiliar to the laity or at best imperfectly understood by them. For this breakdown in communication surgeons in particular, and scientists in general, are not wholly blameless. The general difficulty has been put in its proper perspective by my Principal, Sir Edward Appleton, who remarked in the course of a Graduation Address, "In this connection I believe that a very important factor in the situation is that of communication between the scientist and other members of the community. The scientist must be articulate in the right way. He must be able to expound the results of his work without clouding them in a framework of abstruse phraseology." Nevertheless, in attempting to do so a surgeon would be confronted by a secondary difficulty, which to my mind is at present insurmountable: for while he may (with some trouble) succeed in expounding the results of his work relatively simply in terms of life, health and economic efficiency, he cannot regularly, without recourse to technical terms, explain why he has chosen the particular procedures upon which his results depend.

For a mixed audience, then, the theme had probably better not be surgical, or at least not purely surgical. What choices remain?

THE LIFE OF GREAT PROFESSIONAL ACHIEVEMENT

In a world that has been, from time immemorial, a hero-worshipping world, it is natural that one of the first general topics to suggest itself to a surgeon as to any other orator is the lesson or lessons to be learned from a study of the life and professional achievements of some great man; and in the development of medicine—I use the term in its broadest sense—great men have not been lacking. It is much to be regretted that in this modern world, in which scientific achievement succeeds scientific achievement with a rapidity for which the only appropriate adjective is the platitudinous one of "bewildering," there is an increasing tendency to assess the value of any achievement in terms of present usability. To my mind, this standard is not a desirable one; the absolute measure of the greatness of any achievement should be adjusted to the corpus of knowledge available at the time when the advance was accomplished. However, although it is a truism that all knowledge is progressive, it

is equally true that knowledge cannot progress at the same rate for each one of the arts and for each one of the sciences. In some of the arts, let us say classics or the law, the content of knowledge increases slowly, fields are relatively limited, and possibilities are relatively few. On the other hand, in the physical sciences, and in medicine and surgery, the content of knowledge has often increased by large increments; today these may accrue at short intervals; and fields are boundless and possibilities numberless. Indeed, so rapid is progress in science in this age that each advance—even a modest technical advance — may open up new vistas for exploration. Modern scientific endeavour has this advantage over the work of our ancestors, that almost every day its starting-point is set upon a greater accumulation of knowledge.

Then again, except perhaps in pure mathematics we cannot always measure achievement in terms of absolute rightness or wrongness. Any attempt to do so would at once put a brake upon, or even set a barrier to, progress in every other science. It used to be said that a man could be right or wrong in his opinions, but that no man had the right to be wrong in his facts. What a narrow view this is: for at least in science "facts" are notoriously prone to lose that label in the light of subsequent investigations. On the other hand we must be on guard lest this knowledge engender an attitude of perpetual uncertainty. The prime danger of so extreme an outlook is that it would tend to impede the progress of knowledge by preventing the applications to research of existing hypotheses; it is entirely possible that from such exercises there would emerge, at the least additional observations and at the most modifications or even refinements of the original hypotheses. To be fair, and above all to be rid of the unscientific standards of utilitarianism, it is necessary to enquire whether there are any possible standards for the assessing of an achievement which will overcome the difficulties imposed by the date of its accomplishment, and the impact upon it of subsequent work, standards which will allow a more accurate estimate of real greatness in individuals, particularly in individuals whose lives a surgeon might ask a mixed audience to examine? I feel that there are; and I suggest two criteria for use in so exacting a task.

The first and most important must be the quality of the effort, measured not in terms of mere application, but in terms of imagination and insight. Imagination and insight may have been used in the selection of a new problem for investigation, or (as in the case of Lord Lister) in the choice of a fresh approach to an old problem. The objective need not be one for immediate technical application; although it is quite wrong to exclude work so designed from the highest category of scientific endeavour. Sad to say, the problem may be one whose final elucidation (and possible practical application) the investigator may not live to see. And as there is seldom advancement in one direction without renunciation in another, I may add that the original work, and perhaps even more importantly the hypotheses built upon it, may ultimately prove neither to have been correct in every respect, nor to have had the hoped for applications. I am fortunate in being able to instance, as an example of work of such high quality, the researches of two of your former colleagues, Hunter and Royle. The passage of time has shown that some of their hypotheses were inaccurate; but no one could doubt the quality of work which opened up the field of surgery of the sympathetic nervous system. I am not alone in this opinion; when the late Professor Harvey Cushing was disposing of his private library, he did me the honour of sending me a volume containing the reprints of Hunter and Royle together with his correspondence with them, under cover of a charming letter in which he expressed the opinion that "the volume contained papers which had opened up a new field in surgery, although the precise indications for these operations might be modified by future experience."

The second criterion is the ability to obtain general acceptance of good work, and of the possible applications of that work. It must be admitted that individuals in our profession, sometimes the profession as a whole, and occasionally even learned bodies, have been slow to accept work of a revolutionary character. I introduce this topic with diffidence, because in the address of which I

spoke Trotter remarked that "The text is a favourite one and is apt to become the theme of exhortations which, in addition to having the dreariness of their kind, are pointless because they constitute a frontal attack on an ingrained quality of the mind!" Nevertheless, the matter must be examined briefly, if only because there does not seem to be any single sure tactic for securing acceptance of good work that involves new ideas or fresh outlooks. Both Sir James Y. Simpson, who discovered chloroform, and Lord Lister, who introduced the antiseptic method into surgery, long awaited general acceptance of their contributions to knowledge. Simpson sought it by polemics; he never realized that opposition is not necessarily counter-revolution. Lister sought it by sweet reasonableness; he found it impossible to believe that opposition is not necessarily based on logic. Both men displayed the virtue which is essential in any crusade for recognition, that of moral courage. Yet Simpson, genius though he was, had learned so little from his own experiences that when, ten years later, Lord Lister gave the antiseptic method to the world, he ranged himself with its opponents.

If I may, for a moment, turn from the general to the particular, can we be sure nowadays of the worth of a medical workman and of that of his work? I believe that within recent years this problem—always a controversial one—has been solved for the subjects included in clinical research by the development of the properly controlled trial. The controlled trial may well turn out to be one of the greatest advances of recent years in the practice of medicine. Almost always such a trial, properly designed and preferably conducted with the advice and help of a statistician, will give a clear unequivocal answer as to the worth of any new procedure, and relatively quickly too. I am glad to say that so far as I am aware the best conducted clinical trials in the world are those carried out under the auspices of the British Medical Research Council.

The assessment of new work in the preclinical sciences, and the decision to apply it clinically, are more difficult matters. I know no better rule than Bacon's: "Neither affection for what is new, nor admiration for what is old." The nouns are delicately chosen. *Affection* being an emotion, cannot be expected to be over-critical, and may mistake newness for progress. *Admiration*, being an attitude of mind, may delay advance because it hesitates to give up what was good in its time. I am sure that in Australia you are encouraging and will continue to encourage that mingling of fundamental sciences with clinical science which is currently breaking down the old barriers between them. The more intimate this mixing process, the better does it safeguard really good work in basic science from lack of recognition, or from delay in clinical application.

At this point I realize that I have fallen into a dialectical pit of my own digging: for so far I have defined greatness in terms of achievement alone. And in any audience, whether medical or mixed, there would be a considerable proportion who would object strongly to an estimate of greatness which did not take into account qualities of character and of personality. I am not altogether convinced that this would be a valid objection, because if made it would be an example of a bad habit which is rather a British characteristic, that of constantly obtruding ethics in the wrong places; but I would know that if some insisted upon making it, they would be—as we are in Britain—as uncompromising with themselves as with others. On the other hand, for an orator to praise certain qualities in a personage who might be called a "biotype" of his own choosing would be impertinent, because each member of so distinguished an audience very properly would have his own views on what is laudable in character and personality; and for the speaker to indicate his personal view would be an unforgivable attempt to influence at least the younger members of his audience in the exercise of the most cherished of the freedoms of an educated person. Moreover it may be taken for granted that in a mixed audience such as this, many members have already achieved greatness in different spheres; to suggest to these a limited list of indispensable qualities would be an imposition upon even Australian hospitality. And finally it is I think true that during their lives and as a rule subsequently, almost always estimations of the scientific achievements of individuals are higher than have

been those of their personal qualities; the exceptions are the estimations made by a minority whose personal qualities are the same, or similar.

Is an orator who has taken The Life of Great Professional Achievement to omit that traditional reference to the personal qualities of perseverance and hard work, to which Sir William Osler devoted the whole of a famous address? Decidedly, yes: though they may be suitable themes for adolescents, for adults they are dictatorial and may be wrong. Too many gifted men and women have contributed important advances as the result of intermittent bursts of activity, for perseverance and hard work to be indispensable. Newton was the greatest of all these.

It seems clear then that the topic of the life and achievements of a great man is not entirely suitable for an inaugural address to a mixed audience, because inevitably it raises questions of relative values, for the examination of which the debate is the proper form of exercise, not the address.

THE LIFE OF GREAT SCIENTIFIC INFLUENCE

The next topic which suggested itself was the examination of the qualities and influence of the founder of a school of thought.

It is to be remembered that the founder of a school of thought in any science may have an immense and even dominating influence on its subsequent development; and that this need not necessarily depend upon his personal contributions to knowledge of that science, or to innovations in its practice for which he has been responsible. Medical science is the science above all others in which the importance of a school of thought can be assessed, in large part, by a consideration which must appeal to all thinking people: whether or not it has already modified human experience, or is in process of doing so. Therefore it might be worth while to try to explore the possibilities of such a topic, at least with the lay part of an audience.

As an example of this category, there is no need to look further—and one cannot look higher—than one of the greatest of surgeons, John Hunter. From 1760 onwards Hunter's influence, personal and posthumous, was to change surgery from a craft to a science—slowly at first, then with increasing rapidity. Yet his contributions to the technique of surgery were few.

Hunter began by taking for his studies not man alone, but as much of the animal kingdom as was available to him. To follow such a variety of interests would not be easy for a practising surgeon today. Hunter made himself familiar with the structure of many species, with the function of many of the structures he dissected so painstakingly, and when opportunity offered with processes of disease in various animals.

It is possible to estimate the value of this mass of work by the standards which I have suggested be applied to a single achievement. Thus measured in the light of the knowledge available to him and of the facilities which he could use, his total achievement was stupendous. The quality of the effort he applied to it was exemplary. In his attempts to obtain general acceptance of his work he was hampered by a difficult prose style, and by occasional personal quarrels with colleagues; yet he made converts who became apostles.

Nevertheless neither the volume nor the accuracy of his work is ever sufficient to identify a man as the founder of a school of thought. It is true that inspiration has always rested upon a basis of wide knowledge; an idea cannot be produced nor can a problem be solved by the processes of thought, if the mind has not already stored away all the bits of information required, to await integration. These "bits" may be either pure knowledge, or derived from professional experience: all the bickering about the relative importance of their sources is idle. But only when a man is of sufficient intellectual stature to take what might be called a Pisgah view of his separate inspirations and to generalize from them, can he be considered as the founder of a school of thought.

I return to Bacon for an acute description of this type of great man: "Those who have handled sciences have been either men of experiment or men of dogmas. The men of experiment are like ants: they only collect and use; the reasoners resemble spiders who make cobwebs out of their own substance. But the bee takes a middle course; it gathers

its material from the flowers of the garden, but transforms and digests it by a power of its own. Not unlike this is the true business of philosophy; for it neither relies solely on the powers of the mind, nor does it take the matter which it gathers from natural history and mechanical experiments and lay it up in the memory whole as it finds it; but lays it up in the understanding altered and digested. Therefore from a closer and purer league between these two faculties, the experimental and rational, much may be hoped."

The permanent results of Hunter's labours have been two, the second of which depends on the first: to establish surgery as a branch of biology, and to establish the experimental method as the exact method, not only of assessing surgical procedures, but also of devising them, a gift of vast importance to mankind. The first is a generality, the second provides the generality with concreteness; and as A. N. Whitehead wrote, "Without generality there is no reasoning, without concreteness there is no importance."

Lest the phrase "experimental method" be taken from its context, it is, I think, desirable to examine its connotation in modern times. As applied to the surgeon's work in hospital, it implies the selection of the best procedure from a number of possible procedures for treating a given condition, not by the surgeon's impression, but by the assessment—if possible by accurate measurements in the laboratory — of the deviations from normal function which each process entails, and of the time taken for each process to return to normal. For the aim of all surgery is the restoration of function; and that end-point can be determined—as can end-points in other sciences—by the separation and estimation of all the variables affecting the surgical procedure employed. I need hardly remind you that the surgeon is a doctor too, and treats the patient as a person: but without the application of the Hunterian method, much of surgery would be of necessity empirical. Moreover over-insistence on the art of surgery can lead to a dangerous frame of mind in which the importance of craftsmanship is under-valued.

The term "experimental method" also implies the opportunity of investigating in the laboratory upon animals, under conditions strictly comparable to those of a modern operating theatre, the steps of procedures which may not have been entirely satisfactory in the hospital; and the opportunity of devising new procedures. The propriety of using these opportunities in the laboratory sometimes raises in the minds of laymen an ethical problem, the resolution of which is each person's own affair. My own view, and I think it dispassionate, is that in the interests of my patients I would despair if I had not such opportunities.

There is no doubt that John Hunter's work has profoundly modified subsequent human experience, at least in civilized countries; and that it conformed to the general plan used by all those who have founded schools of scientific thought. Nevertheless, after consideration I felt that to choose the influence of the founder of a school of thought (and in particular that of Hunter) as the topic for my address on this occasion would be to embark on that most unproductive of all efforts, the exhortation of the already converted: for I should have had to deal at length with the importance of the experimental method in surgery, and this I apprehend has always been a tenet of your College.

A THIRD TOPIC

At this point in my address I had set aside the draft for a time: for I was beginning to be bothered by an uneasy feeling that if I continued to search the past for topics I would inevitably come to dregs: and these are unpalatable. And then, in the course of my reading, I came upon not one but (as any experienced surgeon might predict) three statements which led to another approach. The first was by an unknown, and it confirmed my uneasy feeling—"There is no need to drain the dregs of tradition." The second, by Sir George Newman, was that "Other and better men have gone before us, and we enter into their labours; other and better men will follow us and enter into ours." The third—again from an unknown—"We can pay our debt to the past only by putting the future in debt to us." Now to estimate the contributions of this generation to the future of surgery I would have been forced to consider technical matters, and this I had already rejected as undesirable. There remained the dangerous business of attempting to envisage the setting

in which surgery will find itself in the future. One advantage of this choice is that I cannot at once be shown to be wrong, an advantage which has a decided appeal to a Scotsman. But the primary reason which justifies some examination of the subject is that surgery is more and more becoming an integral part of the day-to-day life of any people. This fusion began with the telegraph and telephone, the use of which to summon help or to give advice can be said to have outdone Puck, who could "Put a girdle round about the earth in forty minutes"; and it continued with the rapid development of the internal combustion engine, which has so narrowed the gap between surgeon and patient that it is true to say that there is almost no urgent surgical condition that need kill because of lack of attention: a concept which you here in Australia grasped early, and have turned to bountiful practical application.

There have always been two essentials for the development of any scientific subject—including surgery—and for the smooth application to the common good of each advance as it occurred. They are brains, and adequate facilities; and they are inseparable because interdependent. At least in the case of surgery, to these two must in the future be added a third: a sympathetic public policy, whose only possible secure basis is a sufficient understanding of the breadth of the issues involved. None of these essentials is now, or is ever likely to be, found wanting in Australia; but there is one aspect of the third on which I should like to express a personal view—the *breadth* of these issues.

This matter was brought home to me, rather sharply, when I was reading the autobiography of a distinguished American soldier, General Arnold. "Where are we going?" asked the General. "Only the ancillary scientists of the future can tell us. Let us accept the most fantastic advance we can imagine — are we prepared for its implications?" At the time, I asked a distinguished scientist his opinion of this outlook. His reply startled me. "You could not," said he, "imagine anything sufficiently fantastic."

It is not unknown for the applications of those advances in science which have not been expected by the public to have to await preliminary economic and even political adjustments. I believe that these possibilities pose two problems for future surgery. The first is largely an administrative one. For example, is there any chance that the discovery of a method of curing one of the common killing diseases will find administration at all levels unprepared for that most obvious implication, the rapid increase in population which would follow? And there are other inevitable advances. Bacteriologists and chemists will provide new substances effective in infections which resist those remedies now in use. Pharmacologists will unravel the chemistry of certain glandular disturbances which still require active surgical treatment. The incidence of accidental injuries can be lowered by education, by legislation, and possibly by the further application of industrial psychology. There may be—although this is less likely—some revolutionary addition to the surgeon's technical resources. The realization of any one of these hopes will mean a reduction in the operative work of surgeons, a reduction which they will welcome, for their business is, like that of any other doctor, to restore to health and happiness; and the surgeon does not wish to do this by operation if it can be managed in any other way.

I believe that it would be wise to consider the establishment of something of the nature of a Commonwealth medical general staff to work on plans to meet these and other situations. It might also attempt to devise some method of ensuring that the clinical possibilities revealed by fundamental research were not communicated to the public before they had been passed through that appropriate filter, the controlled trial. Progress is inevitable: one variable is the place where it is made. Thus—in the Hunterian tradition—the net of the planners would have to be cast wide. They might well take note of Huxley's view: "It is a peculiarity of the physical sciences that they are independent as they are imperfect; and it is only as they advance that the bonds which unite them become apparent." If the planners agreed with this view, and I do not see how they could do otherwise, they would devote particular attention to the research conducted in the scientific departments of Universities. Incidentally this attention would encourage the breaking down of the few remaining

interdepartmental barriers. The knowledge gleaned from it, and from all the many other fields of endeavour which such a staff would keep under review, would then be examined as a whole. In this last step—and I believe it would be extremely productive—in this last step only those of the highest intellectual qualities and of the broadest of outlooks should be concerned.

The second problem is educational. It will be clear that in the future much is to be hoped from the marriage — polygamous I fear — between clinical surgery and the ancillary sciences: between Royal Colleges and Universities. The linkage might properly begin in undergraduate years: students of to-day will be at the height of their powers in the next generation, when it may well be that the practice of surgery will be greatly changed by advances in the fundamental sciences. The breadth of the issues requires, on the one hand, an early student appreciation of such possibilities: and how better can this be ensured than by following the advice of G. M. Young, that "In every department a lecture should occasionally be given by a student in another department: so that everyone should have some experience in conveying in the language of common discourse ideas which are usually expressed in technical language." On the other hand, the breadth of the issues requires—ideally it is true—that teachers should have the outlook of the next generation but one. To achieve these ends it is essential that University departments devoted to the ancillary and preclinical sciences should have at their disposal ample funds for purposes of fundamental research: and that there should be an interchange of clinical experience and of technical innovations on the broadest possible basis, preferably by such personal contacts as have been made possible by the wise generosity of Sir Arthur Sims.

The professional bodies, the Royal Colleges, will of course have with the Universities the natural linkage of a common objective—the advancement of the science of medicine. Their obligations in maintaining the academic standards of practice are long-established and salutary, and need not detain us. But in a future in which spectacular changes may crowd upon one another I foresee for them a particular and perhaps in some ways the decisive responsibility: for Royal Colleges are the repositories of experience; and from experience it is possible and desirable to distil wisdom. And the wise, and only the wise, should be allowed to decide the series of choices which will inevitably confront surgery, each of which may be reduced to the same simple terms: whether a procedure which is presently possible is ultimately desirable. On the correctness of their decisions will depend both the good name of surgery and the retention of a sympathetic public policy. Both these objectives should commend themselves to each member of a mixed audience.

These reflections on the choice of a topic for an inaugural address have been of necessity incomplete, nor has it been possible to examine the suitabilities of more than two or three subjects. But I am left with the conviction that on such occasions—even though they be annual—it is better to look forward than to look back; to look ahead for new opportunities for putting the more distant future in debt to us, to try to surmise how these may be encouraged, and to try to envisage how they may be fitted into the future pattern of our lives. In the last analysis, it is a forelock that Time wears, and to seize it is the entirely proper ambition of each one of us.

Now, Sir, I ask your leave to depart from my theme, and, since this is an inaugural address, to speak my closing words to the younger Fellows of this College who are inaugurating their life's work: for they alone will have the opportunity of judging of the correctness of the excursion into "the dreaming" upon which I have ventured.

The younger Fellows:

You have privileges provided on the one hand by the availability of knowledge accumulated over the years throughout the civilized world, and on the other hand by that impetus towards progress which is the hall-mark of virile countries. "These Australians," writes Sir Ernest Barker of those of fifty years ago, "these Australians had sunshine in their veins: they bubbled with ready fun: they blew into the antiquity of

Oxford with the challenge of their own and their country's youth." The Australian has not changed. But the challenge is now to him, and it should be met in Australia.

It is the spirit of Syme that throws down the gauntlet to you. As you press forward to take it up, I respectfully offer to you two pieces of advice: one old, one not so old.

The old is the shrewd admonition of Bacon: "Noble inventions may be lying at our very feet, and yet mankind may step over without seeing them." In this great country, oppo- tunities for the finest of all temporal ques will always be yours for the seizing.

The new is the verse which Poet Laureate Masefield is said to have taken as his own guide, and to have passed on to those seekin his advice about their future:

"Sitting still and wishing,
Makes no person great;
The good Lord sends the fishing,
But you must dig the bait."

EXTRAVASATION OF BILE AFTER OPERATIONS ON THE BILIARY TRACT

GRAHAM MCKENZIE

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THE disclosure of an intraperitoneal collection of bile, either following abdominal trauma or as a sequel to suspected or obvious inflammatory conditions of the biliary tract, has been a matter for report by contemporary surgical writers (Fifield, 1926; Newell, 1948; Moore, 1950). In addition, the surgical literature contains many reports of cases of "spontaneous bile peritonitis," a condition as cryptic in its clinical manifestations as it is devastating in its general effects (McWilliams, 1912; Buchanan, 1918; Cope, 1925).

However it is rather surprising to find that there are relatively few authoritative surgical presentations which deal with bile extravasation into the peritoneal cavity following operations on the gall-bladder and bile ducts. Douglas and Grey Turner (1940), reporting three cases of bile extravasation after cholecystectomy, comment on the lack of published observations on the clinical course of post-operative bile leakage.

Bile peritonitis is usually described in surgical literature as producing diffuse abdominal pain, tenderness and rigidity, and a varying degree of shock. This is an accurate description of the state of a patient who has suffered traumatic rupture or inflammatory perforation of the biliary tract, but it does not often fit the patient who has developed an extravasation of bile after cholecystectomy. While leakage of bile into the peritoneal cavity after operation may cause sudden collapse of the patient, with obvious signs of an intraperitoneal catastrophe, it more commonly produces a less dramatic onset and follows an insidious course. Failure to appreciate this fact results in the diagnosis of bile extravasation being rejected in a patient whose post-operative course is not proceeding smoothly, on the grounds that definite signs of peritonitis are absent. The patient "does not seem to be sick enough" to warrant such an unpleasant diagnosis. Absence of the "classical" signs of bile peritonitis is responsible for delay in diagnosis and treatment. This procrastination results at least in a prolonged stay in hospital, and sometimes in the death of the patient.

The present report is based on the personal observation of eight cases of post-operative extravasation of bile, supplemented by examination of the records of another twelve patients.

THE SITE OF BILE LEAKAGE

Theoretical considerations suggest the following possible causes of bile extravasation:

1. Slipping of the ligature on the cystic duct.
2. Operative damage to the hepatic or common bile ducts.
3. Leakage from accessory ducts which have been divided without being recognized during the dissection of the gall-bladder from the liver.
4. Escape of bile after accidental dislodgment of a drainage tube which has been placed in the common bile duct.
5. Seepage of bile through a suture line in the common bile duct.

Actually it is often impossible to determine the site of leakage. This is particularly the case at laparotomy where the surgeon will be anxious simply to drain the collection without prolonging the operation to search for the source of the bile. Even at autopsy however, there may be difficulty in locating the site of leakage.

In 12 of the 20 patients studied no source could be found.

In the remaining 8 cases the cause of the extravasation was apparent and the findings are set out in Table 1. It will be seen that in all but two cases the leakage was from

TABLE 1

SITE OF BILE LEAKAGE IN EIGHT CASES

Case	*Site of Leakage*	*Cause*	*Extravasation found at*
1	Common bile duct	Tube dislodged from it on second post-operative day	Autopsy
2	Common bile duct	Tube removed on tenth post-operative day. Healing of external fistula but bile continued to collect within peritoneal cavity	Operation
3	Common bile duct	Common duct explored and closed without drainage. Leakage of bile through suture line. No drainage through tube in Morison's pouch	Operation
4	Common bile duct	Leakage through site of needle puncture in operative cholangiogram	Operation
5	Cystic duct	Ligature slipped from cystic duct	Autopsy
6	Common bile duct	Common duct explored and closed without drainage. Leakage of bile through suture line. No drainage through tube in Morison's pouch	Autopsy
13	Accessory duct	Probable cholecyst-hepatic duct in gall-bladder bed, not obliterated by oversewing of bed	Autopsy
17	Common bile duct	Common duct divided at cholecystectomy	Operation

the common bile duct. Certain features are worth noting:

1. In two cases leakage occurred through the suture line in the common bile duct. Bile accumulated within the peritoneal cavity in spite of the presence of a drainage tube in Morison's pouch. No bile escaped through this tube in either patient.
2. One patient had a long standing obstruction of the common bile duct due to a carcinoma of the head of the pancreas. At operation a cholangiogram was performed, the opaque medium being injected through a needle inserted into the common bile duct. After this a cholecyst-jejunostomy was carried out. A drainage tube was placed in Morison's pouch. Several pints of bile escaped through the needle puncture wound in the common duct after operation and although some of this emerged through the drainage tube the greater part remained in the peritoneal cavity. Operative evacuation was necessary.
3. In one case the presence of an accessory duct was postulated by the pathologist who had identified at autopsy an area in the gall-bladder bed from which bile was oozing freely. Such an accessory duct was found in a patient who is not included in this series and is shown in Fig. I. It was displayed in the course of dissecting the gall-bladder from the liver and was divided deliberately without ligation. Bile ran freely from the hepatic end. It was therefore clamped and ligated and in this patient there was no post-operative extravasation. However such a duct could be overlooked. Even where no duct of this size is present, oozing of bile from multiple small ducts in the gall-bladder bed is a possible explanation of the extravasations for which no source can subsequently be found.

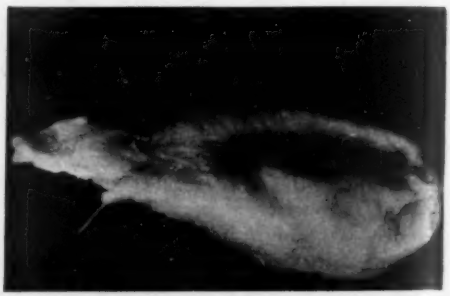

FIG. I. Photograph of gall-bladder showing accessory duct.

CLINICAL FEATURES

Douglas and Grey Turner (1940) suggested that cases of bile peritonitis fell into two groups, one comprising patients with a localized collection of bile shut off from the rest of the peritoneal cavity and the other consisting of patients in whom a diffuse peritonitis developed. This observation is confirmed by a study of the location of the

bile collection in the patients whose histories are considered in this paper. But it is at once apparent that the clinical presentation and course of bile peritonitis are not necessarily related to the extent of the extravasation or to the degree of its localization. On theoretical grounds it seems reasonable to assume that those patients with a large generalized extravasation would present an acute onset and thereafter a rapid deterioration in their condition. On the other hand one would expect those patients with a localized collection to be characterized by a more insidious onset, slower development and a more favourable prognosis. That this is not necessarily so, may be seen from consideration of the histories of these patients.

From the clinical point of view it is apparent that patients suffering from post-operative extravasation of bile fall readily into two groups.

The first group comprises those patients in whom the onset is dramatic and the course rapid. The striking feature in such cases is the sudden collapse of the patient early in the post-operative course. Shock overshadows all other features and it is this which distinguishes them from the second group.

The second group consists of patients in whom the bile extravasation produces symptoms and signs of variable severity without any evidence of shock. The variation in the clinical presentation of patients in this group is considerable. At one extreme are those whose general condition remains good but whose symptoms and signs nevertheless constitute a clear indication for laparotomy. At the other extreme are those patients in whom the onset is so mild and the subsequent course so insidious that there is considerable delay in the establishment of a diagnosis of bile extravasation.

The clinical features of these two groups are illustrated by the patients who have been studied.

GROUP 1

Patients having an acute onset with shock

Seven patients have been placed in this group and their main features are summarized in Table 2.

TABLE 2

MAIN FEATURES OF CASES HAVING ACUTE ONSET AND COURSE

Case No.	*Sex*	*Age*	*Original operation*	*Outstanding feature of onset*	*Pain*	*Abdominal signs*	*Time between onset and operation or death*	*Findings*	*Treatment*	*Result*
6	F	48	Cholecystectomy Choledochotomy	Collapse 48 hours after operation	Upper abdominal	Generalized tenderness	12 hours	At post-mortem: generalized extravasation	Nil	Death
8	F	38	Cholecystectomy Choledochostomy	Collapse 12 hours after operation	Right hypochondrium and right shoulder	Nothing definite	24 hours	At operation: localized collection under liver	Drainage	Recovery
13	F	50	Cholecystectomy	Collapse 30 hours after operation	Absent	Distension	24 hours	At operation and post-mortem: generalized extravasation	Drainage	Death
14	M	60	Cholecystectomy	Collapse 30 hours after operation	Absent	Distension	24 hours	At operation: localized collection under liver	Drainage	Recovery
15	F	74	Cholecystectomy	Collapse 48 hours after operation	Absent	Mild distension	24 hours	At post-mortem: localized collection under liver	Nil	Death
16	M	59	Cholecystectomy	Pain and collapse 20 hours after operation	Severe generalized abdominal	Generalized tenderness and rigidity	48 hours	At operation and post-mortem: generalized extravasation	Drainage	Death
18	M	48	Cholecystectomy	Collapse 48 hours after operation	Absent	Mild distension	12 hours	At post-mortem: localized collection under liver	Nil	Death

Shock was the outstanding feature and in all patients it was of gross degree. It developed within forty-eight hours of operation. Pain was not necessarily present and in only one case was there severe generalized abdominal pain. Abdominal signs were indefinite. Rigidity was found in only one patient. Tenderness was marked in this case but in the others was not a prominent feature. It is obviously difficult to assess the significance of tenderness in a patient with a recent abdominal wound.

Mild distension of the abdomen was noted in some cases.

The following case history illustrates the clinical features and course of patients in this group.

Case 13

Mrs. E.P., aged 50 years, had a cholecystectomy performed on the 27th November, 1952. A fibrosed gall-bladder containing stones was removed, a small fistula between the gall-bladder and duodenum being divided. The duodenal defect was invaginated and oversewn. The common bile duct was not opened. A drainage tube was placed in Morison's pouch.

The following day, the abdomen was somewhat distended and the pulse rate had remained elevated since operation. It was recorded as 120 per minute but the pulse volume was good. That evening the patient vomited and was found to be in a state of circulatory collapse. She had made no complaint of pain. There had been no drainage from the tube since operation. The abdomen was distended and silent, with mild generalized tenderness.

Resuscitative measures were instituted and during the next eight hours her condition improved. The wound was then reopened and approximately three pints of bile were evacuated from under the right lobe of the liver. The source of the bile could not immediately be identified and in view of the patient's poor condition, no prolonged search for it was made. A large drainage tube was placed in Morison's pouch and the abdomen was closed. The patient died six hours later.

At autopsy, the peritoneal cavity was found to contain two pints of bile-stained fluid. The common bile duct was intact and the ligature on the cystic duct was still in place. There was no leakage from the duodenum. There was a general oozing of bile from the gall-bladder bed and one point was located from which there seemed to be more leakage than elsewhere. The presence of a cholecyst-hepatic duct was postulated, although it was not possible to demonstrate it with certainty.

GROUP 2

Patients having a sub-acute or insidious onset and course

It is in this group that the greatest difficulties in diagnosis arise and this justifies a careful examination of the clinical presentations of the patients studied. Thirteen patients have been placed in this group and their main features are summarized in Table 3.

Shock

No signs of shock were observed in any of these patients. It was noteworthy that the patient's general condition was maintained throughout a long period during which the bile extravasation was present, even though in some cases it caused quite severe symptoms.

Latent period

One of the most striking features of the patients in this group was the period of time during which the bile collection must have been present without any symptoms developing. Although many developed symptoms within four or five days of operation, there were others who made no complaint for periods ranging from one to four weeks after cholecystectomy. Douglas and Grey Turner (1940) record one case in which symptoms did not develop until several weeks after operation and the bile collection was evacuated six weeks after cholecystectomy. James (1938) described a patient who developed the first symptoms six weeks after operation. In only one case of the present series was the interval as long as this, but in several it was sufficiently long to indicate that a bile extravasation may be tolerated for a surprisingly long period.

Pain

Abdominal pain was a feature in more than half the cases. The onset was usually sudden but the severity was variable. It was usually of short duration and in those patients who were not submitted to laparotomy, the pain subsided within a few hours. However further attacks occurred. The pain was located either in the epigastrium or right hypochondrium and in some cases was referred to the right shoulder as well. It was

TABLE 3

MAIN FEATURES IN CASES HAVING A SUB-ACUTE OR INSIDIOUS ONSET AND COURSE

Case	Sex	Age	Original operation	First symptoms after operation on:	Pain	Vomiting	Abdominal signs	Pulse Rate per minute	Jaundice	Chest signs	Time from onset to operation or death	Findings at operation or post-mortem	Treatment	Result
1	F	69	Cholecystectomy Choledochostomy	6th day	Absent	Moderate	Distension	120	Mild	Present	15 days	Localized collection under liver	Nil	Death
2	F	38	Cholecystectomy Choledochostomy	30th day	Severe upper abdominal in bouts	None	Tenderness during attacks	100+ during attack	Mild with last attack	Absent	60 days	Localized collection under liver	Drainage	Recovery
3	M	42	Cholecystectomy Choledochostomy	2nd day	Sharp pain in right hypochondrium and right shoulder	None	Absent	116	Absent	Present	14 days	Localized collection in right anterior subphrenic space	Drainage	Recovery
4	M	49	Cholecyst-jejunostomy Operative cholangiography	2nd day	Absent	None	Distension	100	Present before operation	Absent	3 days	Large generalized extravasation	Drainage	Recovery
5	F	53	Cholecystectomy Choledochostomy	6th day	Short attacks in epigastrium and right shoulder	Moderate	Distension in terminal stages only	Elevated in terminal stages only	Present before operation	Present	23 days	Generalized extravasation in loculi	Nil	Death
7	F	70	Cholecystectomy Choledochostomy	2nd day	Recurrent epigastric	None	Rigidity during first attack of pain	Not elevated at early stage	Absent	Absent	5 days	Localized collection under liver	Drainage	Recovery
9	F	30	Cholecystectomy Choledochostomy	22nd day	Mild constant epigastric	Moderate at onset	Tender in epigastrium	100+	Absent	Absent	3 days	Localized collection under liver	Drainage	Recovery
10	F	50	Cholecystectomy	5th day	Absent	None	Mild distension	140	Mild	Absent	2 days	Localized collection under liver	Drainage	Recovery
11	F	69	Cholecystectomy	4th day	Sharp pain in right iliac fossa and right shoulder	None	Tenderness in right iliac fossa	120	Absent	Absent	8 hours	Localized collection right side of abdomen	Drainage	Recovery
12	F	42	Cholecystectomy	5th day	Absent	Moderate	Moderate distension	110	Mild	Absent	3 days	Localized collection under liver	Drainage	Recovery
17	F	38	Cholecystectomy	24th day	Recurrent mild epigastric	Moderate at onset	Marked distension	116	Absent	Absent	4 days	Generalized extravasation	Drainage	Recovery
19	F	62	Cholecystectomy	6th day	Recurrent in right hypochondrium	None	Absent	Not elevated	Absent	Present	4 days	Localized collection under liver	Drainage	Recovery
20	F	43	Cholecystectomy	3rd day	Recurrent in right hypochondrium	None	Tender in upper abdomen	120	Absent	Absent	6 hours	Generalized extravasation	Drainage	Recovery

usually associated with some localized tenderness but rigidity was found in only two patients. It is significant that in several cases there was no complaint of pain.

Vomiting

This occurred in a few cases but was not severe. However the patients began vomiting several days after operation, when there was no question of its being due to a post-anaesthetic disturbance. Vomiting at this stage should not be disregarded.

Distension

Some degree of abdominal distension was observed in approximately half the group.

Jaundice

Four patients who had not been jaundiced before their original operation, developed mild jaundice after the extravasation of bile. But seven patients with a collection of bile in the peritoneal cavity did not develop jaundice at any stage.

Pulse rate

Elevation of the pulse rate was noted in the majority, and in several it was found that there had been a persistent tachycardia from the time of operation, although the significance of this was not realized until other signs were present.

Chest signs

James (1938) reported the presence of signs at the base of the right lung in his case of post-operative bile extravasation. It is significant that in four of the cases of the present series, deterioration in the patient's condition was ascribed to a pulmonary lesion. Signs found at the base of the right lung were attributed to either a segmental collapse or an infarct, and treatment was initially directed to these conditions. In two of them, the primary lesion under the diaphragm was demonstrated at autopsy. In the others, the lung signs disappeared after drainage of a collection of bile which had extended into the right anterior subphrenic space.

Drainage after the original operation

In many cases there was no record as to the amount of drainage after the original operation. However, among the patients whom I observed personally, there were two findings which were considered to be significant. In some there was no drainage of any kind from the tube during the first forty-eight hours after operation. On the other hand, in two patients, there was a copious drainage of bile during the first two days and then the outflow suddenly ceased. It is usual for the drainage after cholecystectomy to consist of slight blood-stained discharge, rapidly becoming serous and ceasing within forty-eight hours. Sometimes there is slight bile-staining of the dressings. Complete absence of discharge or excessive bile drainage both represent a departure from "normal" and the significance of this will be discussed when diagnosis is considered.

It has already been stated that there was considerable variation in the severity of the symptoms and signs in the patients included in this sub-acute or insidious group. Some of them presented an onset and course which might well be classified as acute, but they have not been included in the acute group because of the absence of shock. However, their symptoms and signs were sufficiently definite to make it clear that the abdomen should be re-opened. The following is an example of such a case.

Case 11

Mrs. F.B., aged 69 years, had her gall-bladder, with its contained stones, removed on the 30th May, 1952. The common bile duct was not opened. The abdomen was closed with a drainage tube in Morison's pouch. There was some bile-stained drainage from the tube during the next forty-eight hours. This tube was removed on the third post-operative day.

The following day, she complained of a sharp pain in the right iliac fossa, the pain being first felt as she was being assisted to her bed after sitting out in a chair. When examined, she was tender in the right lower abdomen. The pulse rate was 120 per minute but the volume was good. No abnormality was found on examination of the chest. Four hours later, the abdominal pain was less severe although she complained of some pain in the right shoulder.

She was examined again eight hours after the onset of her pain. The pain had subsided completely but there was still tenderness in the right iliac fossa, and the pulse rate had not decreased. The abdomen was therefore reopened, and a gush of purulent bile followed the opening of the peritoneum. This outflow was from a collection mainly under the right lobe of the liver, but extending down into the right iliac fossa. After evacuation of as much fluid as possible, drainage tubes were placed in Morison's pouch and in the pelvis. The source of the bile leakage was not found.

Her recovery was uneventful and she was discharged three weeks after cholecystectomy.

On the other hand, where the symptoms and signs were less definite, and the course more insidious, there was delay in treatment which had serious consequences in more than one case. The following patient is an example.

Case 5

Mrs. R.F., aged 53 years. Cholecystectomy and exploration of common bile duct on the 9th July, 1952. A "T" tube was placed in the duct and a large drainage tube in Morison's pouch. She made satisfactory progress until the sixth post-operative day, when she complained of some pain in the right shoulder. It was not severe. The following day, she had an attack of pain in the epigastrium and vomited twice. The pain subsided, but she complained of discomfort on breathing during the next twenty-four hours. Diminished air entry at the base of the right lung was noted, also the presence of moist sounds. X-ray examination of the chest and diaphragm did not show anything significant. In the next two days, there was some improvement, but on the tenth day after operation, she developed sudden pain in the epigastrium. At this time a diagnosis of bile extravasation was considered, but the pain abated rapidly, and her general condition remained good. Because of this, the decision to re-open the abdomen was deferred. From this time until the twenty-first post-operative day her general condition remained satisfactory but every two or three days she complained of short attacks of abdominal pain situated now in the lower abdomen. Her general condition then deteriorated rapidly, this change being accompanied by some further vomiting and the appearance of abdominal distension. She developed peripheral circulatory failure and died twenty-nine days after operation.

At autopsy, there was an extensive extravasation of bile due to slipping of the ligature from the cystic duct. There were numerous adhesions throughout the peritoneal cavity dividing the bile collection into many loculi.

The insidious course which may be followed even when a large extravasation is present is well illustrated by another patient.

Case 12

Mrs. A.M., aged 42 years, was first seen on the 17th May, 1953. Her gall-bladder had been removed seven days before. The common bile duct had not been explored. There had been a fairly copious discharge of bile from the drainage tube in Morison's pouch during the first thirty-six hours. This tube was removed forty-eight hours after operation. Her temperature had fallen to normal after the second post-operative day, but the pulse rate had remained between 90 and 100 per minute. On the fifth post-operative day, she had vomited several times and mild abdominal distension had been noted. The following day, she felt better after a bowel action. The stools were normal in colour. However, the conjunctivae were seen to be slightly icteric and although her general condition was good, it was feared that some intraperitoneal complication had occurred.

When seen on the 17th May, 1953, she complained only of recurrent nausea. The pulse rate was 110 per minute. There was a mild degree of jaundice. The abdomen was slightly distended but soft. There was some tenderness in the vicinity of the incision but it was not deemed to be of consequence.

A diagnosis of bile extravasation was discussed, but in view of her good general condition and the absence of any signs of peritonitis, laparotomy was deferred. The next day however, there was further vomiting and it was decided to re-open the abdomen.

Four pints of bile were evacuated from under the liver. The gall-bladder bed was inspected and appeared to be dry. The cystic duct ligature was seen to be intact and the common bile duct normal. No further bile seemed to be collecting and the abdomen was closed with a large drainage tube in Morison's pouch. Bile drained copiously from this tube for several days then suddenly ceased. Her recovery was uneventful.

Two patients illustrated the fact that normal convalescence may occur in spite of the presence of an extravasation of bile. In both cases, symptoms developed after their discharge from hospital.

Case 2

This patient was discharged from hospital apparently well two weeks after cholecystectomy and choledochostomy. Four weeks after operation, she had an attack of severe upper abdominal pain which she described as being similar to biliary colic. It subsided in a few hours but she had two further attacks at intervals of one month. With the last of these, she became jaundiced. At laparotomy a small collection of bile was found under the liver. She recovered after drainage and has remained well.

Case 17

This patient was admitted to the Royal Melbourne Hospital four weeks after cholecystectomy performed elsewhere. She was stated to have made an uneventful recovery from this operation. Four days before admission, she began vomiting and developed abdominal distension. A large collection of bile was evacuated at operation. Subsequently, it was shown to have come from a complete division of the common bile duct. Bile extravasation must therefore have taken place immediately after cholecystectomy, but it had produced no symptoms for four weeks.

DIAGNOSIS

In these cases delay in diagnosis was common. Not unexpectedly the delay occurred mainly in cases of the insidious type, and in some of these the diagnosis was not made during life. Excluding patients whose bile collection was found post-mortem and also those who first developed symptoms when

they were no longer in hospital under observation, it is seen that the period from onset of symptoms to diagnosis in the insidious type of case ranged from eight hours to fourteen days, the average time being four days.

In cases of the acute type, who develop peripheral circulatory failure in the first forty-eight hours after operation, a diagnosis of reactionary haemorrhage or of bile extravasation will be immediately considered. Laparotomy will be undertaken if possible, with suitable resuscitative measures. But it is important to realize that such a dramatic onset is seen in less than half the patients who develop a post-operative leakage of bile. An early diagnosis in all cases will only be made if it is appreciated that the symptoms and signs may be mild and fleeting in the early stages. Pain, even though it may be mild and of short duration, should arouse suspicion. Unexplained tachycardia or the development of vomiting and abdominal distension several days after operation may be due to an intraperitoneal collection of bile. In a patient showing any of these features, the record of drainage after operation should be carefully considered. A drainage tube from which there has been no outflow at all has almost certainly been blocked by blood clot or an omental plug from the beginning and therefore fails to indicate an intraperitoneal accumulation of bile. More significant still, a copious discharge of bile, ceasing suddenly before or after removal of the tube, shows that an abnormal exit from the biliary tract exists. The development of any abdominal symptoms and signs in such a case would constitute strong evidence of an intraperitoneal collection.

Two special measures may help in diagnosis:

1. X-ray examination: In a patient in whom signs are found at the base of the right lung, impaired movement or elevation of the right half of the diaphragm on X-ray examination may be due to a subdiaphragmatic collection of bile.
2. Paracentesis abdominis: This has a limited use. It was performed in two patients of this series because there were signs of free fluid in the abdomen. In one patient no fluid was obtained but in the other bile was aspirated through a needle inserted in the left flank.

In an extensive extravasation with signs of free fluid in the abdomen, this procedure is justifiable. More often however, the bile collection is situated in the right upper abdomen and needling of this region would not be free of risk, since post-operative adhesions may cause bowel to be perforated by the needle.

After operations on the biliary tract, any abdominal abnormality, whether of acute or of insidious onset, should suggest the possibility of leakage of either blood or bile from the site of operation. If the surgeon adopts this attitude, he will be less likely to defer the reopening of the abdomen. In cases of bile extravasation it may well be a life-saving operation.

PROGNOSIS

This aspect is considered in regard to 20 patients in whom a post-operative extravasation of bile was discovered at operation or autopsy. There were 7 deaths.

Of the patients who developed sudden peripheral circulatory failure in the first forty-eight hours after operation, only 2 of 7 survived. Of the thirteen patients who have been classified as having an insidious onset and course, eleven recovered, all after operative evacuation of the bile.

Although the numbers are small, the mortality of those patients having an acute onset suggests that the prognosis is bad when the extravasated bile induces a state of shock, whether or not resuscitation and evacuation of the bile is carried out. In those in whom the condition develops insidiously, without any initial general disturbance, it is more difficult to estimate the outcome. Obviously, the results with drainage in these cases are good. The only two deaths in this group were in cases where drainage was not carried out. But the series is a selected one and includes only cases in which the diagnosis was made by opening the abdomen. It is possible that cases occur in which there is an extravasation of bile and subsequent absorption. The patient may have unexplained

symptoms and signs of a mild nature during the post-operative period but finally recover completely. That this is possible, is suggested by the following case history:

Case 3

Mr. N.H., aged 42 years. At operation on the 10th February, 1954, a thick-walled gall-bladder containing multiple small stones, was removed. Small stones were felt in the common bile duct which was not dilated. The duct was opened and the stones removed. A sound passed easily into the duodenum. As there was no evidence of obstruction of the common bile duct, the incision in it was closed by suture and a large drainage tube was placed in close proximity.

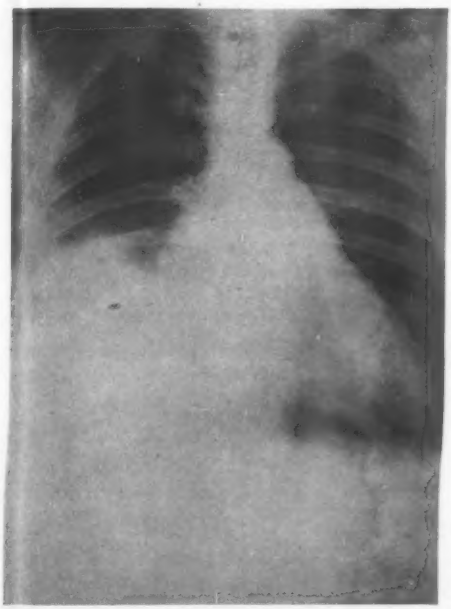

FIG. II. X-ray of patient (Case 3) showing elevation of right side of diaphragm due to subdiaphragmatic collection of bile.

In the first twenty-four hours after operation, a small amount of bile escaped from the tube. Drainage then ceased. Eight hours later, the patient complained of pain in the region of the wound and in the right shoulder. A probe was passed along the drainage tube to see if it was kinked and this was found to be the case. By loosening the tube and withdrawing it a short distance, the kink straightened and bile flowed from the tube. A few hours later, the patient said all his pain had gone.

He made good progress until seven days after operation, when he developed sudden stabbing pain under the right costal margin, intensified by breathing deeply. His temperature was 101° and his pulse rate 116 per minute. On examination of the chest, there was dullness on percussion of the base of the right lung and no breath sounds were heard below the level of the spine of the scapula. The abdomen appeared to be normal. Recurrent stabbing pains were felt for several hours after which he stated that he felt better.

Over the next few days, his temperature fell to normal but the chest signs persisted. X-ray examination showed considerable elevation of the right half of the diaphragm and appearances suggested a small collection of fluid in the pleural cavity (Fig. II).

He appeared to be improving, but in view of the persistent lung signs and the X-ray appearances, it was considered that he had a collection of bile under the diaphragm. Therefore on the 24th February, 1954, the previous incision was reopened. On top of the liver there were adhesions which were broken down to permit entry into a cavity with bile-stained fibrin-covered walls. There was very little fluid in the cavity, which was estimated as being of five or six ounces capacity. Normal healing had taken place in the region of the gall-bladder bed and bile duct. The cystic duct ligature was intact. A tube was left in the cavity for forty-eight hours and there was slight bile-stained discharge from it. Thereafter, recovery was uneventful.

Drainage of this cavity was undertaken at a stage when the patient was showing clinical improvement. However, experience of previous cases suggested that temporary improvement could occur even in the presence of a large extravasation of bile. There was considerable evidence of bile extravasation having occurred in this patient. It was therefore thought wise to perform laparotomy. However, in view of the evidence provided by operation, it is probable that this patient would have recovered without further interference.

It is impossible to say how often absorption of such a bile collection occurs. Certainly a critical examination of the patients reported here provides adequate evidence that failure to evacuate extravasated bile usually results in persistent morbidity and gradual deterioration.

Only 2 patients of the 13 having an insidious course were not treated by evacuation of the bile and both developed a sudden terminal circulatory failure. At this stage, operation would offer no prospect of saving the patient's life. Therefore, it seems reasonable to assume that without early re-drainage of the abdomen the prognosis in post-operative bile extravasation is bad.

Of the patients who recovered after drainage, only 6 have been seen since, at intervals varying from three months to two years after operation. None of them has had any further symptoms referable to the complication of bile peritonitis.

TREATMENT

Prevention of a bile extravasation obviously depends on meticulous adherence to well-known principles in the technique of cholecystectomy and choledochostomy. The cause of bile leakage in those cases of this series in which it is known emphasizes the need for secure ligation of the cystic duct, proper oversewing of the gall-bladder bed, and careful closure of any incision in the common bile duct. Drainage of the common duct is obligatory if it is opened in the presence of obstruction, and this has been shown to apply even when the opening consists only of needle puncture of the duct.

In one patient, the drainage tube in the common bile duct was accidentally dislodged on the second post-operative day. Drainage of bile continued through the tube in Morison's pouch, but it was insufficient to prevent the accumulation of a large sub-hepatic collection which was found post-mortem. Accidental dislodgment of a common duct tube in the first two days after operation, before adhesions have formed a well-defined track, may therefore be a serious matter. Later in the post-operative course, accidental dislodgment is unlikely to have serious consequences, but the experience in this patient suggests that if the tube is displaced in the first forty-eight hours, an operation to replace it should be undertaken.

The failure of the Morison's pouch drainage tube to permit the escape of bile is illustrated by several of these cases. Usually this will be due to blockage of the tube by clot and debris, but in one patient it was thought to be due to kinking. This was believed to result from the fact that the tube's point of emergence through the abdominal wound was at such a level that the tube was kinked by the costal margin once the patient assumed a sitting position, even though it was well clear of the ribs when he was recumbent. This explanation may be correct and it suggests the desirability of always bringing this tube out through a stab wound well below the costal margin.

Although not referable to any of the cases reported here, it is worth recording that a bile extravasation has been seen following the use of a rubber glove to collect bile from a drainage tube in the common bile duct. The glove was emptied, and then re-applied to the tube, but was tied too tightly onto it with obliteration of the lumen. Collection of the bile into a bottle seems to be a safer procedure.

Once extravasation is suspected or known to have taken place there is no question that the bile should be evacuated and drainage of the abdomen should be re-established. One case in the series showed the possibility of absorption of the bile and it may well be that other bile leakages are dealt with by natural processes. But in patients in whom there are clinical signs consistent with accumulation of bile within the peritoneal cavity, the only safe course is to re-open the abdomen and evacuate the collection.

SUMMARY

1. The clinical features of post-operative bile extravasation have been described, based on a study of 20 patients suffering from this complication.

2. The source of the bile leakage was undetermined in 12 cases. In the remainder the sites of leakage have been set out.

3. The patients have been divided into two groups according to their clinical course. Seven patients suddenly developed shock in the first forty-eight hours after operation, and five of these died within twenty-four hours of the onset, in most cases before any surgical treatment could be undertaken. The other group comprises thirteen patients who ran a course which was more benign, but nevertheless insidious in that diagnosis was often delayed because of the mildness and remittent nature of the symptoms and signs. Two of these patients died without the diagnosis being made. The remainder recovered after operative evacuation of the bile.

4. The clinical presentation did not seem to be necessarily related to the extent of the extravasation or to its degree of localization.
5. Delay in diagnosis was common, particularly in the patients who had an insidious onset and course. It is suggested that in such cases there should be no hesitation in performing laparotomy as a diagnostic procedure if there are reasonable grounds to suspect extravasation.
6. Treatment is discussed from the point of view of prevention. Once an extravasation of bile is present, its early evacuation, with drainage of the abdomen, is the correct treatment.

ACKNOWLEDGEMENTS

I wish to thank the Honorary Staff of the Royal Melbourne Hospital, where the majority of these cases was seen, for permission to report them; and the Honorary Staff of Prince Henry's Hospital for access to the records of other patients who have been included.

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MEGAURETER WITH VESICO-URETERIC REFLUX IN TWINS

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In a previous paper (Stephens, 1954) the clinical and radiological features of bilateral ureteric dilatation (idiopathic megaureter) in children were described, and it was shown that these cases may usefully be divided into two groups, those with and those without vesico-ureteric reflux.

In the reflux group, free regurgitation of urine from the bladder up both ureters occurred during micturition, the ureters being full after complete emptying of the bladder. The ureteric reflux emptied back into the bladder after two or three minutes, and the urinary tract could be completely emptied by two or three efforts at micturition at two minute intervals. This procedure has been termed "triple micturition." It serves effectively to remove residual urine, and thus prevent urinary infection. The emptying times of the ureters of these patients were within normal limits, indicating that obstruction at the lower ends of the ureters is not a factor in the production of this type of megaureter.

In the second group without reflux, micturition cysto-urethrography demonstrated a normally acting bladder and urethra with complete emptying of the bladder, but with no vesico-ureteric reflux. After retrograde pyelo-ureterography it was observed that there was delay in emptying of the ureters, the contrast medium being still present in the ureters up to six and seven hours after retrograde injection. In this group, unlike the former group, it therefore appears that obstruction at the lower ends of the ureters may play a part in the development of megaureter. It is possible by vesico-ureteroplasty to induce free ureteric reflux, so that the urinary residue can be removed by "triple micturition" as in the first group of children. Only two cases have been treated by this technique and regime, and the follow up is too early to assess results.

The pathogenesis of these conditions is not fully understood. In the previous study one of a pair of monovular twins with megaureter with reflux was described. Since then the co-twin of this child has been investigated, and also a second index twin with megaureter and her binovular co-twin have been examined. Both index twins had megaureter with vesico-ureteric reflux and neither presented evidence of obstruction at the uretero-vesical junction. This paper reports the findings in these children, and discusses the genetic background and pathogenesis of this type of megaureter in the light of these findings. We have not been able to find any previous reports of congenital megaureter in twins in the literature, although Mackay (1945) reported a family in which three siblings had congenital megaureter and hydronephrosis, but without vesico-ureteric reflux. It is not possible, however, on the information quoted, to exclude the possibility of ureteric stricture being present in these children.

Reports of Cases

Twin Pair 1

D.A. and W.A. are twin girls born on 11th September, 1946.

D.A. had an attack of pyuria at the age of two years, and persistent pyuria for five months from the age of five years nine months, at which time her weight was 34½ lbs. and blood pressure 120/70 mm. of mercury. At this time, and again eight months later, micturition cysto-urethrography showed free reflux up both ureters, though more freely up the left side than the right. There was complete emptying by "triple micturition." The ureters were shown to have a larger calibre than normal and were slightly tortuous. For two years she has practised "triple

*Working with the aid of a grant from the National Health and Medical Research Council of Australia.

micturition" and has been free of urinary tract infection, although at the time of writing there has been a recurrence of infection due to a breakdown of the regime. At seven years two months her weight was 38¼ lbs. and height 45¾ inches. Her blood pressure on 23rd June, 1954, was 120/80 mm. of mercury.

W.A. has had no known urinary infections. At seven years two months her weight was 39½ lbs., and her height 46 inches, her blood pressure was 120/80 mm. of mercury on 23rd June, 1954. A micturition cysto-urethrogram on two occasions has shown free reflux up the left ureter, which is hardly above normal calibre. Intravenous pyelography reveals normal kidneys, and shows that the right ureter is normal in calibre, while the left is of high normal calibre and uniformly smooth in outline. There was no reflux up the right ureter, which in her twin D.A. allowed reflux less freely than the left.

Twin Pair 2

S.M. and J.M. are twin girls born on 16th January, 1948.

S.M. was first examined on 2nd March, 1953, with a history of anorexia, languidness and pallor for two months, and dysuria for two weeks since receiving a kick in the abdomen at school. On examination she was pyrexial (103°F) with a tender, palpable bladder and pyuria. After treatment, the urinary infection recurred. On 13th November, 1953, intravenous pyelography revealed a normal left pyelogram and slightly enlarged left ureter, a small right kidney with bunching of the calyces and a large calibre right ureter. Renal function on the left side was better than on the right. Micturition cysto-urethrography on 20th November, 1953, showed free reflux up both ureters, the right being larger and permitting reflux more freely than the left. The bladder emptied completely and all residual urine could be removed by "double micturition." No further infection has occurred since "double micturition" has been instituted. On 24th November, 1953, her weight was 42½ lbs. and her height 44 inches.

J.M. has had no infections of the urine or serious illness. On 24th November, 1953, her weight was 32½ lbs. and her height 41 inches. Micturition cysto-urethrography and intravenous pyelography have shown no abnormality in the urinary tract.

TWIN STUDIES

The first twin-pair, D.A. and W.A., were considered on clinical grounds to be monovular (identical) twins, as they were extremely similar in height, weight, appearance and behaviour. The second twin-pair, S.M. and J.M., on the other hand, were dissimilar in size, appearance and behaviour, and were considered to be binovular (non-identical) twins.

These conclusions were confirmed by blood group studies performed by one of us (R.T.S.). The blood groups of the first pair of children were the same for all seven independent groups tested, as determined by the use of specific and potent testing antisera, while those of the second pair showed unequivocal differences in two blood group systems (Table 1).

TABLE 1

The seven blood groups of the twin pairs. The first pair D.A. and W.A. show identical results, while the second pair S.M. and J.M. differ in the M-N-S and K groups.

Twin Pairs	Group						
	A-B-O	M-N-S	Rh	P	Le^a	Fy^a	K
D.A.	A1–2	Nss	Rh_1Rh_2	+	−	−	−
W.A.	A1–2	Nss	Rh_1Rh_2	+	−	−	−
S.M.	A1	Ns	Rh_1Rh_2	+	−	+	−
J.M.	A1	MNS	Rh_1Rh_2	+	−	+	+

DISCUSSION

Vesico-ureteric reflux does not occur in normal children. In over 200 micturition cysto-urethrograms performed by one of us (F.D.S.), reflux has been seen only in megaureter, and to a slight degree in the terminal one-quarter of the normal calibre ureters in the high tension infantile bladder enuretics (Higgins, Williams and Nash, 1951). This reflux disappears with training of the bladder and cure of the enuresis. Reflux may also occur in the late stages of urethral obstruction, and in certain neurological lesions such as spinal meningo-myelocoele. In all of these cases except idiopathic megaureter the reflux may be adequately explained.

In idiopathic megaureter with vesico-ureteric reflux the present evidence suggests that the abnormality lies in the ureterovesical junction, and possibly to a variable degree in the ureter above, and that the abnormality permits varying degrees of reflux during micturition.

Conversely, in megaureter without reflux, the mechanism at the vesico-ureteric junction may be overactive, preventing reflux and hindering efflux, as measured by the delayed emptying times of the ureters, resulting in

obstructive megaureter. Division of the localized intramural segment by vesico-ureteroplasty renders this mechanism inefficient, converting this type clinically into the reflux type. The urinary tract may then be emptied by "triple micturition." It remains to be seen, in two cases recently treated, whether the children do empty their urinary system completely by this means, and whether they are symptom free after alleviation of the obstruction. In both types the uretero-vesical junction is abnormal, and in the obstructive type the megaureter is presumably secondary, while in the reflux type it is not certain whether the megaureter develops as a result of the reflux or as a congenital anomaly.

The presence of reflux in both D.A. and W.A., who are monovular twins, but its occurrence in only one of the binovular twins S.M. and J.M., is presumptive evidence that the condition is a genetically determined and not an acquired anomaly. It is also noteworthy that in both the monovular twins the reflux was greater on the left than on the right side.

It is also considered for two reasons that the calibre of the ureter is not entirely dependent on the freedom of reflux at the uretero-vesical junction:

(a) The calibre of the ureters with very free reflux may be hardly above normal in one child, but large or gross in others.

(b) In some children, where the reflux into the lower ureters is free on both sides, the calibre of both ureters is different.

The genetic factor which affects the vesico-ureteric mechanism may thus also affect the calibre of the ureter.

The role of infection must also be considered. When bilateral reflux and pyuria are present it is assumed that both ureters are infected, yet one ureter may be smaller in calibre than the other, and may permit reflux only into the lower end of the smaller ureter. Micturition cysto-urethrograms performed more than six months after cessation of infection in the monovular twin D.A. showed no change in calibre. In the series reported, five cases, whose urinary tracts had remained clear on "triple micturition" were re-examined by the cysto-urethrography technique between six and seventeen months later. The calibre in three was unchanged, and in two only slight decrease had occurred. Infection thus seems to have little effect on the ultimate calibre of the ureters or the degree of reflux in the majority of cases, although it is the chief cause of symptoms.

It would thus appear that the abnormality of idiopathic megaureter with reflux combines a congenital absence or partial absence of the mechanism which prevents vesico-ureteral reflux and which regulates the entry of urine into the bladder from the ureter, with an enlargement of the ureter which is probably also a primary anomaly. The twin studies suggest that this anomaly is genetically determined in cases with vesico-ureteric reflux, and the family described by Mackay (1945) points to a similar explanation in megaureter without reflux.

SUMMARY AND CONCLUSIONS

1. Vesico-ureteric reflux with megaureter has been observed in both of a pair of monovular twins, but in only one of two binovular twins.
2. The anomaly may be due to a genetically determined change affecting the mechanism of the uretero-vesical junction and possibly the calibre of the ureter.
3. Although the cause of symptoms, urinary tract infection does not greatly affect the ultimate degree either of reflux into or dilation of the ureter.

ACKNOWLEDGEMENTS

In addition to the acknowledgements made in the previous paper (Stephens, 1954), we would like to record our gratitude to Dr. H. G. Hiller, Director of the Department of Radiology, Royal Children's Hospital, for his co-operation in these studies.

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THE JUGULAR BODY AND ITS TUMOUR

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"TUMOUR" formation has been now described in most of the non-chromaffin paraganglia, one of the most recently recognized tumours being that arising from the *glomus jugulare* or jugular body.

It is proposed to record in this paper 11 new jugular body tumours, together with a brief consideration of the normal organ. A hitherto unknown portion of the jugular body is described.

The Jugular Body

The normal jugular body was first mentioned as such by Guild (1941) whose description is worth quoting. "Human temporal bone sections reveal structures in several respects like the carotid body for which the name *glomus jugularis* is proposed. Usually they are in the adventitia of the dome of the jugular bulb, immediately below the bony floor of the middle ear and near the *ramus tympanicus* of the glossopharyngeal nerve. Usually there is but a single flattened ovoid glomus about 0.5 mm. in the longer diameters and about 0.25 mm. thick. Occasionally about two or more smaller bodies are present, sometimes one or all are in the canal that transmits the *ramus tympanicus* through the floor of the middle ear (in one case also along the course of this nerve over the cochlear promontory)."

"Each glomus, wherever located, consists of blood vessels of capillary calibre with numerous epithelioid cells between the vessels. Usually, but not always, the vessels are the more prominent feature. Innervation and blood come from the same trunks that supply the carotid body, namely, the glossopharyngeal nerve and the ascending pharyngeal artery."

It may be pointed out here that Krause (1878) wrote: "On opening up the *canalis tympanicus* of a human temporal bone, it will be observed that there is a fusiform swelling of the tympanic nerve where it has entered the canal after leaving the petrous ganglion. This swelling measures 4 mm. long and 1 mm. thick . . . It is highly vascularized, consisting of a basic framework of connective tissue with elastic fibres, containing a network of arteries, veins and capillaries." He noted a resemblance to the carotid body and named the structure the tympanic body.

Guild (quoted by Capps, 1952), since his paper of 1941, notes further that:

(i) the bodies occur along the auricular branch of the vagus as well as the tympanic branch of the glossopharyngeal nerve;

(ii) slightly more than half of the bodies are in the adventitia of the dome of the jugular bulb;

(iii) along the tympanic branch a glomus formation may be present, distal to its promontorial part in the region where the nerve becomes continuous with the lesser superficial petrosal nerve near the geniculate ganglion of the 7th cranial nerve;

(iv) along the auricular branch of the vagus a glomus formation may be present at least as far distally as where the mastoid canaliculus crosses the descending part of the facial canal.

Zettergren and Lindström (1951) sectioned 10 temporal bones and were able to find the organ or portions thereof in 9; in 50 per cent. of cases the main mass of the body was found in the adventitia of the jugular vein. Lattes and Waltner (1949) noted these bodies as multiple nests of carotid body-like tissue not only in the adventitia of the jugular vein but also along the tympanic nerve in its bony canal and in the promontory very close to the middle ear.

The present writer has sectioned serially one temporal bone through the dome of the jugular bulb as the centre of the section, the block of tissue being pared down to a size

2 x 1½ x 1½ cm. before cutting on the microtome. Four other temporal bones have been sectioned, using the jugular ganglion of the vagus nerve as the centre of the section.

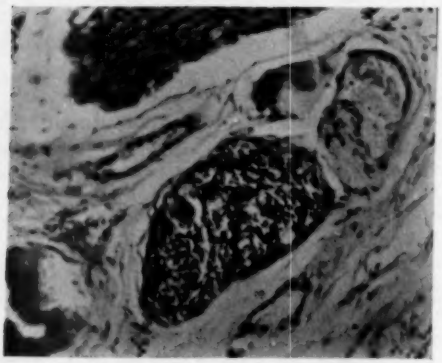

FIG. I. Photomicrograph of a portion of the jugular body in the canal of the tympanic nerve, portion of which is seen above. (x 180)

In the sections from the first temporal bone, nests of cellular tissue, closely resembling the carotid body, have been seen in the adventitia of the jugular vein and also in the canal of the tympanic nerve (Fig. I). Each nest of tissue measures .5 to .8 mm. in its longest diameter and presents a structure almost identical in ground plan and blood supply with that of the carotid body.

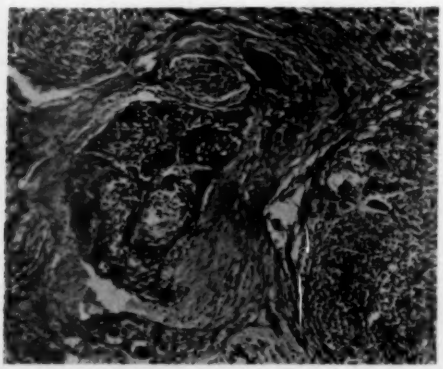

FIG. II. Photomicrograph of a new non-chromaffin paraganglion situated in jugular ganglion of vagus nerve. This is quite separate from the paraganglion already described in the ganglion nodosum of the vagus nerve. (x 90)

In each of the 4 temporal bones in which the jugular ganglion of the vagus nerve was sectioned, a nest of carotid body-like tissue was found. This was situated towards the centre of the ganglion, between the bundles of nerve fibres and ganglion cells (Figs. II, III and IV).

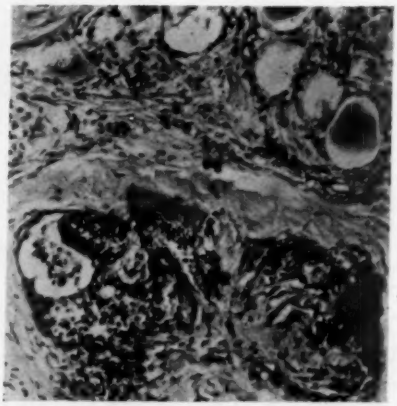

FIG. III. Photomicrograph of another jugular ganglion of the vagus nerve showing ganglion cells (above) and a nest of jugular body tissue. (x 180)

All the bodies found had a similar glomerular structure and consisted in section of a number of endothelium-lined fine vessels separated by a small amount of collagen tissue and large epithelioid cells with round or ovoid nuclei. A number of ganglion cells, as noted by Lattes and Waltner (1949), has been seen (Fig. V). The nerve supply appears to be sensory in type as in the carotid body, ring-shaped nerve endings being apparent in contact with the epithelioid cells.

Nomenclature is still a problem. Krause (1878) named the portion he discovered the tympanic gland whilst Guild (1941) used the term *glomus jugularis* as an inclusive designation. Berg (1950) prefers the term tympanic body for two reasons: first, the priority of Krause's discovery and secondly the intimate relation of the separate portions of the organ to the tympanic branch of the glossopharyngeal nerve.

However, in the light of our present incomplete knowledge, together with the description in this paper of another vagal paraganglion, it is perhaps best to retain the non-committal term jugular body as indicating the general area in which portions of this tissue may be

found. The term jugular body does not commit us to a functional interpretation—this is most desirable when it is remembered that it is only by virtue of morphological similarity that the jugular (and also the vagal body) is grouped with the carotid and aortic bodies as the chemoreceptor system. This premature functional interpretation has already been extended by the use of the ungainly word "chemodectoma" (Mulligan, 1950) for a tumour arising from any of the constituent parts of this system of non-chromaffin paraganglia.

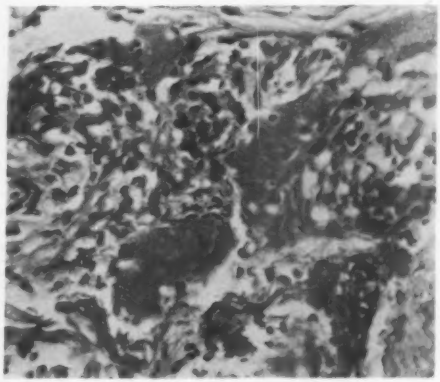

FIG. IV. High power photomicrograph of portion of Fig. II showing the glomerular structure. (x 380)

Recently Smetana and Scott (1951) have claimed the discovery of a non-chromaffin paraganglion in the thigh situated in the femoral canal. This has been invoked to explain the histogenesis of a frankly malignant tumour, the granular cell myoblastoma of the thigh (Smetana and Scott, 1951; Randall and Walter, 1954). The writer does not consider the evidence sufficient to justify this conclusion.

On the other hand it is noteworthy that in the mouse, some 13 portions of non-chromaffin paraganglionic tissue have been described along the course of the vagus nerve below the diaphragm (Goormaghtigh, 1936). It is therefore reasonable to expect that further portions of non-chromaffin paraganglionic tissue will be described in the human being.

Much work has been done on the physiology of the chemoreceptor system but, to the present time, the only pathological change of importance described is that of tumour formation. It is conceivable that this dearth of pathological information may be due to lack of simple morbid anatomical investigation. A glaring illustration of this is the statement that the carotid body is present in only about 25 per cent. of human beings (MacComb, 1948). Thus, the present writer has been able to disprove this assertion by demonstrating the carotid body in each of 100 consecutive autopsy cases, the body being identified macroscopically in 85 cases.

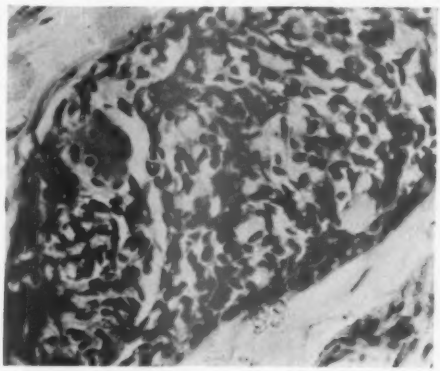

FIG. V. High power photomicrograph of the paraganglion seen in Fig. I. A large ganglion cell may be seen. (x 380)

THE JUGULAR BODY TUMOUR

In 1945, Rosenwasser, while describing a tumour of carotid body-like nature in the middle ear, suggested an origin from the jugular body. Today there are nearly 100 records of jugular body tumours or non-chromaffin paragangliomata in the literature. However these are mainly in American and Scandinavian journals and until very recently (Capps, 1952; Magarey, 1952; Black, 1952; Gaffney, 1953; Bickerstaff and Howell, 1953) the condition had been somewhat neglected by English clinicians and pathologists.

It is clearly desirable that these tumours should be more widely and more easily recognized: first, so that we may know more of their history and behaviour, thus assisting development of a method of treatment, and secondly, because of the variety of ways in which they may first present for treatment.

TABLE SHOWING DETAILS OF

Case No.	*Sex*	*Age*	*Main Symptoms*	*Duration on First Presentation*	*Side*	*Cranial Nerve Palsies*	*External Meatus*	*Middle E*
1	M	30	Deafness, pain, discharge from ear, buzzing in ear	6 weeks	L	5, 7, 8	Large aural "polyps" which recurred after each curettage	Filled by mas vascular tissue
2	F	67	Aching pain in ear	2½ years	R	8	Eardrum occluded by "raspberry-like" nodule	—
3	F	36	Deafness and buzzing noise in ear. Recent haemorrhage from the ear	4 years	R	7, 8	Small pulsating nodule in floor of external meatus	Filled with ex vascular tumo
4	F	35	Buzzing noises in ear and discharge; recently noticed deafness	6 years	L	8	Fungating vascular mass in floor of external meatus	Filled with pul tumour tissue
5	F	31	Deafness, headache and facial weakness	2½ years	R	7, 8, 12	Sessile smooth solid vascular tumour in floor of external meatus	—
6	F	27	Headaches and recurrent blurring of vision (papil-loedema) and buzzing in ear. Recent deafness and atrophy of right side of tongue	6 years	R	8, 12	Pulsating vascular tumour on posterior portion of drum	—
7	M	32	Deafness, buzzing noises in ear and facial weakness	9 years	R	7, 8, 10	Pink tinge of drum with injected vessels	Large encapsu pulsating mass bedded in right petrous tempo
8	F	56	Haemorrhage and discharge from ear	7 years	R	8	Vascular polyp in external meatus	—
9	F	40	Wasting of tongue, weak voice, difficulty in swallowing and deafness	4½ years	L	8, 10, 11, 12	Pink tinge of drum	—
10	F	55	Buzzing in ear and haemorrhage	—	R	8	Vascular mass in right meatus	
11	M	42	Deafness and buzzing in head, some pain and recent haemorrhage	5 years	R	8	Bluish polyp in right external meatus which bled on touching	—

S OF JUGULAR BODY TUMOUR

Biopsy	Treatment	X-ray Appearance	Remarks
...ar connective ...gio- ...oma	Radical mastoidectomy 1934 and 1940—recurrence after each. Pain relieving operations since	Accoustic meatus, interior of mastoid and petrous temporal appear as if dissolved out. Angiogram shows many new vessels replacing left petrous bone	Recent lumbar puncture CSF 400 mgm. Protein, pressure 200 mm. water. Alive 19 years after the onset of the disease and presentation
...ous tumour	Nil	Blurring of mastoid air cells	Alive 4 years after presentation with recent attack of labyrinthitis. Pulsatile vascular tumour present in external meatus
...ssue only	Ligation of external carotid artery	Blurring of mastoid air cells	Alive 5 years after initial onset of disease. No buzzing noises
...oma	Radical mastoidectomy with recurrence 3 years later	Blurring of mastoid air cells with erosion of bone in middle ear area	Alive 22 years after initial onset of symptoms; tumour still present but extent not known
...oma	Nil	Area of erosion apparent in petrous temporal	Alive 6 years after initial onset with symptoms and signs as at presentation
–	Ligation of external carotid artery and radio-therapy	—	Alive 9 years after initial onset of symptoms with no headache and buzzing in ear much reduced
–	Ligation of external carotid artery, craniotomy	Gross erosion of petrous temporal and adjacent occipital bone with almost complete obliteration of the jugular foramen	Alive 14 years after initial onset. Buzzing in head much reduced by ligation of carotid. Intracranial spread proven by craniotomy 7 years after onset
...olyp ...body tumour	Nil	Area of erosion apparent in petrous temporal	Alive 8 years after onset of disease. Hypertensive
–	Craniotomy	Bony defect in left jugular fossa extending into petrous temporal and adjacent part of occipital bone	Alive 5 years after onset of symptoms. Intracranial growth 3 cm. in diameter located in region of jugular fossa. CSF pressure and protein normal
...oma	Radical mastoidectomy with profuse bleeding	Blurring of mastoid air cells with some destruction of petrous temporal	Death from cerebral abscess following mastoidectomy. Autopsy showing intracranial spread on inner surface of petrous temporal; middle ear, Eustachian tube and mastoid region involved; spread apparent in transverse sinus. Cerebral abscess and bronchopneumonia caused death
...oma	Ligation of common carotid	Erosion of petrous temporal	Death from cerebral infarct. Autopsy showed intracranial spread on inner surface of petrous temporal. Mastoid region and middle occipital bone involved. Tumour present in jugular vein and sigmoid sinus

The main features of the present series of 11 cases are summarized in the Table and some of these features will now be discussed.

Clinical aspects

Eight of the 11 patients are females, a predominance of females in accord with the experience of previous writers. The average age at the time of presentation is 41 but it should be remembered that the history may be of a number of years' duration before the patient first presents.

In any consideration of the symptomatology of these tumours the scattered distribution of the constituent portions of the jugular body should be remembered as a possible explanation for the diversity of modes of presentation. Thus, if the tumour arises in the region of the jugular bulb, the initial symptoms will be due to a mass in the external meatus and middle ear while a deeper origin in the temporal bone may produce facial palsy, nerve deafness and vestibular symptoms. Occasionally, as in Case 6, the main complaints will be those due to intracranial extension.

The common presenting symptoms are deafness, buzzing in the ear which may be noted, by an intelligent patient, as synchronous with the pulse, pain, haemorrhage, otorrhoea which may be purulent and any one of a number of cranial nerve lesions. Vestibular disturbances have been rare in the present series.

In every case except 2 (Cases 7 and 9) a vascular polypoidal mass was present in the floor of the external meatus; usually this was noted as pulsatile. Case 7 showed only a pinkish colouration of the drum while Case 9 showed no abnormality in the ear; in both these cases gross intracranial spread was demonstrable. Case 6 is rather unusual in that the patient presented several times, in the six years preceding the development of any other symptoms or signs, with papilloedema and raised cerebrospinal fluid pressure. Neurological signs appear almost invariably in late stages of the disease but in several of the cases in this series gross neurological signs have been present at the first examination.

Various combinations of from the 7th to the 12th cranial nerve lesions may be found whilst in Case 1, with a history of at least twenty years' duration to date and admittedly far advanced, the 5th nerve had been severely affected.

In 6 cases of the series a loud bruit was a source of much discomfort and considerable annoyance to the patient.

There have been 2 deaths in this series, in each case following operative interference; reference will be made to this later. All other cases show well the long clinical course which is apparently characteristic of these "tumours," patients in Cases 1 and 4, for example, being alive some twenty years after the initial onset of symptoms.

Radiological aspects

As there are difficulties and, indeed, dangers inherent in the taking of an adequate biopsy of the growth, radiological examination assumes great importance from both diagnostic and prognostic viewpoints.

FIG. VI. Skiagram of an advanced jugular body tumour (Case 7) showing the dissolution of the left petrous temporal bone characteristic of the disease. The large bony defect in the cranium is operative in origin.

In all cases in this series changes were seen on radiological examination although in Cases 2 and 3 blurring of the mastoid air cells, comparable with that of a chronic mastoiditis, was the only finding. In all other cases actual destruction or erosion without any sign of bony reaction was the

prominent feature. In Case 7, for example, the appearance was reported "as if the petrous temporal bone had been dissolved out" (Fig. VI). In other cases erosion was also obvious in adjacent portions of the occipital bone.

Angiography, from a review of the recent literature, has given conflicting results. Thus, vertebral angiography in the hands of Riemenschneider *et alii* (1953) has been of value while Henson *et alii* (1953) report disappointing results from both carotid and vertebral angiography. In this series where carotid angiography was done (Cases 1, 7, 8 and 9) and the external carotid artery filled with dye, much of the petrous temporal became opaque, indicating a very vascular tumour. There are, however, variations from this appearance which have been dealt with in detail by Hooper (1954). Filling of the external carotid artery in angiography is essential, as the blood supply of the normal body arises from this vessel. A fact pointing to confirmation of this is that in Cases 3, 6, 7 and 11 ligation of the external carotid artery either greatly reduced or completely eliminated troublesome buzzing in the ear.

Pathological aspects

There is no doubt that the sites of origin of these tumours, in so far as this can be ascertained, may be correlated with the sites in which the normal jugular body tissue is found. Thus some 50 per cent. of recorded tumours appear to arise in the region of the jugular bulb, presenting via the middle and external ears. The remainder arise along the course of the tympanic branch of the glossopharyngeal nerve, the auricular branch of the vagus and as far afield as the geniculate ganglion of the facial nerve. Thus there may be no tumour apparent in the external ear or even in the middle ear.

Growth of the mass is largely by radial expansion, perhaps best appreciated on radiological examination where the area of bone affected has undergone complete resorption. Since growth by slow expansion is easiest along natural pathways, the jugular foramen, transverse sinus and auditory canals are particularly liable to be involved with subsequent cranial nerve palsies.

The autopsies performed on Cases 10 and 11 in this series illustrated the modes and routes of growth very well. For example, Case 10 showed tumour in the transverse sinus and jugular bulb, while Case 11 showed tumour tissue in the transverse sinus, jugular vein and internal auditory meatus. In both cases the tumour projected intracranially from the posterior aspect of the petrous temporal bone. In addition, in Case 11 tumour was apparent in the occipital bone behind the mastoid process. The actual destruction or erosion of bone can be compared with that produced by, for example, a cavernous haemangioma or lipoma of the scalp and not an expression of malignant invasion *per se*.

Macroscopically the tumour remains confined beneath a capsule, and within the meatus, beneath the stratified squamous epithelium lining the external meatus. In Case 11 the comment was made that the tumour in the transverse sinus was extremely firm.

Occasionally following surgical interference, particularly in the external meatus, the tumour becomes ulcerated and infected. Haemorrhage almost always follows. On cut section the colour is usually reddish-brown but may be grey. The tissue is always excessively vascular, particularly at the periphery of the mass. During every attempt at surgical interference, premeditated or emergency, the oozing is commented upon and in several cases haemorrhage became so severe that operation had to be stopped. The vascularity of the peripheral portion of the tumour is usually obvious on superficial inspection, the mass in the external meatus being pulsatile and synchronous with the carotid pulse. Leashes of vessels are also obvious in intracranial extensions of the growth. The blurring of the mastoid air cells seen on radiological examination in early cases is probably due to an accompanying mastoiditis.

Histologically a wide variety of appearances have been described by various writers. This diversity of histological structure has again been noted in the fragments available for section in the present series but it is probable that, were a whole specimen available for examination, they could all be found in the

one tumour. The best material here was that from the autopsies on patients in Cases 10 and 11.

The overall histological pattern in section is of large polyhedral epithelioid cells arranged in groups, distinguishable among thin-walled endothelium-lined vessels (Fig. VII). In parts the tumour cells may be arranged in cords or clusters separated by thin-walled sinusoidal vessels (Fig. VIII). The protoplasm in most cells in haematoxylin and eosin-stained sections is slightly granular whilst, in some, it is clear and homogeneous. Cell borders often are ill-defined. Nuclei stain well and show nucleoli. In the section from the patient in Case 11 giant cells with bizarre-shaped but single nuclei were seen; no mitosis was observed.

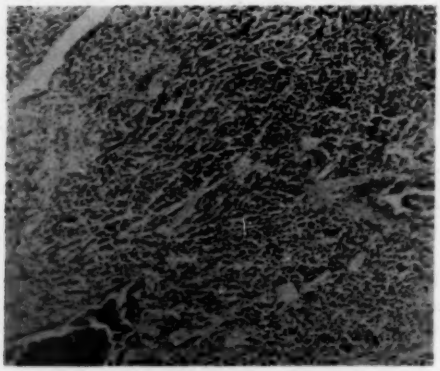

FIG. VII. Lower power photomicrograph of a jugular body tumour showing the general cellular appearance. The vascularity of the tumour is obvious (Case 11). (x 60)

It should be noted here that distant metastases were not demonstrated in either autopsy case.

Where biopsy material only is available, the picture histologically is apparently much more diverse, since a local peculiarity becomes very prominent. Thus, if the biopsy be taken from the surface of the vascular mass in the external meatus, the appearance commonly is that of a modified granulation tissue (Fig. IX). Other areas, particularly those deeper in the tumour, may show predominantly fibrous tissue (Fig. X)—a common finding in both the carotid and vagal body tumours (Birrell, 1952, 1953). Again very vascular areas may be seen, the appearance suggesting, at first sight, some form of angioma or endothelioma.

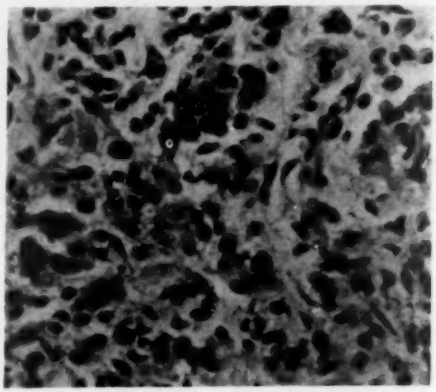

FIG. VIII. High power photomicrograph of a jugular body tumour showing a rather pleomorphic cellular picture with, however, a glomerular arrangement characteristic of the normal body (Case 11). (x 380)

Attempts were made with the material available, to demonstrate a "nerve supply" similar to that found in the carotid body tumour (Birrell, 1952). Some success has been achieved using Willis's (1954) stain for nervous tissue. Large nerve trunks have been found running in the fibrous tissue septa (Fig. XI) while varicose fibres similar to those demonstrated in the carotid body tumour have also been demonstrated in the fibrous septa (Fig. XII). No "nerve supply" to the parenchymal cells of the tumour has been demonstrated, despite the close resemblance of the parenchyma of the tumour to the normal body's parenchyma; previous experience has shown that one needs a fortunate section for this purpose.

It is somewhat more difficult to assess the pathological status of the present series of tumour than for the carotid and vagal body tumours. By virtue of their site of origin they are much more difficult to treat surgically and to thereby remove them completely. From the viewpoint of their pathological nature, their well-differentiated structure, lack of mitoses, slow growth, encapsulation and lack of distant blood-borne metastases are points which indicate a hyperplasia rather than a neoplastic process.

FIG. IX. Low power photomicrograph of a superficial portion of a jugular body tumour obtained by biopsy of a polyp in the external meatus. Some tumour is apparent below but it is easily seen how the true diagnosis may be missed (Case 8). (x 180)

Prognosis

It has been said of patients with carotid body tumours that their greatest danger lies in treatment rather than the disease itself (Pettet *et alii*, 1953). This stricture may be applied much more rigidly to cases of jugular body tumour. The 2 deaths in the present series followed directly upon operative intervention, one patient (Case 10) from a cerebral abscess and bronchopneumonia following radical mastoidectomy while another (Case 11) died of cerebral infarction following ligation of the internal carotid artery. Similar statements appear accompanying many case reports in the literature. "In many cases no doubt the tumour outlives its host who dies from other causes" (Black, 1952). In justification of this last statement is the fact that case histories of twenty years or more duration are well known. Indeed, 2 cases of the present series have been living for about twenty years even though one patient did have a radical mastoidectomy early in the progress of the disease.

Prognosis in untreated cases is reasonably good since patients may live for many years even with multiple nerve palsies and gross destruction of the petrous temporal bone. Aural symptoms, usually the initial ones, commonly precede neurological signs and symptoms by some years and it may be another few years before definite signs of bony erosion become apparent on radiological examination.

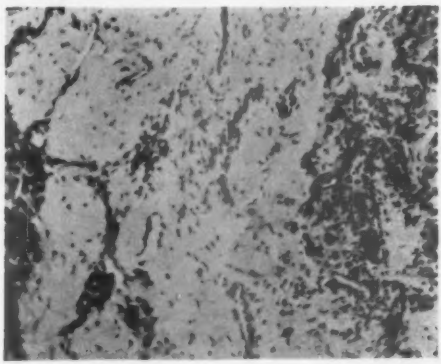

FIG. X. Low power photomicrograph of a portion of a jugular body tumour (Case 1). Fibrosis is apparent and little organized tumour tissue is present in the section. (x 180)

Treatment

At the outset it can be stated that no specific line of treatment has yet emerged. From a consideration of the organoid structure of the tumour itself, its lack of mitoses, slow growth rate and also by analogy with its near relative the carotid body tumour one would not expect radiotherapy to be effective. Henson *et alii* (1953) claim its use in one case with success while Alexander and Adams (1953) report a case two years after apparently successful radiotherapy.

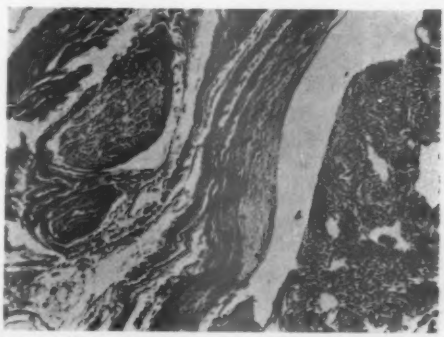

FIG. XI. Low power photomicrograph of a portion of a jugular body tumour (Case 10) showing on the left of the illustration, two large nerve bundles lying in a fibrous septum between tumour masses. (x 30)

It has been used several times in this series and in one case, together with ligation of the external carotid artery, has produced obvious benefit. However, it is realized that the essentially long natural history of the tumour makes any assessment of its value difficult.

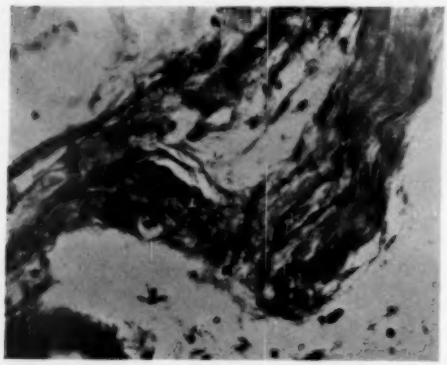

FIG. XII. High power photomicrograph of several nerve fibres showing varicosities. The fibres are running in a fibrous septum (Case 10). (x 380)

Regarding the tumour as a hyperplastic process affecting all or some of the constituent portions of the jugular body, complete surgical removal as in the case of the carotid body would be curative. The main difficulty lies in the great number of anatomically important structures in this area, but a further difficulty is that most patients show radiological evidence of bone destruction on first presentation indicating almost certain irreparable damage to structures such as nerves. In other words, to effect complete removal would require not radical but heroic surgery. It must also be remembered that patients with this disease may live, in the absence of treatment, with only minor or moderate inconvenience for a number of years.

Several radical mastoidectomies were performed on cases in this series (recurrence has been invariable) the operations usually being emergency in nature following a curettage or biopsy which resulted in severe haemorrhage.

One procedure which has been of value in eliminating a bruit which is troubling the patient is ligation of the external carotid artery; this has been of particular value in Case 7. It is possible that this may also slow the growth of the tumour or even cause some regression.

DISCUSSION

As far as aural growths are concerned jugular body tumours must be regarded as comparatively common so that it is essential that both clinicians and pathologists be aware of this entity.

It will be noted that in only 7 of the tumours recorded here has a biopsy been taken. The reason for this lack of material is that the task of obtaining an adequate biopsy from these tumours either by the aural or the intracranial route is a procedure of considerable gravity. This is underlined by the fact that radical mastoidectomy had to be performed in 4 cases following biopsy, there being no other method of stopping the resultant haemorrhage. There is also recorded in the literature a number of these involuntary mastoidectomies.

Hence biopsy of a suspected jugular body tumour should only be undertaken with both operative and resuscitation facilities immediately available. Two further important points regarding biopsy are mentioned by Magarey (1952). First, if only a superficial portion of a tumour be submitted for histological examination the diagnosis may well be missed when only granulation or inflammatory tissue is seen; secondly, all aural polyps should be submitted for histological examination.

The present series showed in its sex incidence the definite predominance of females which is so far unexplained. Thus Capps (1952) reviewing 58 cases from the literature notes an incidence of 82.7 per cent. in females. This may be compared with the carotid body tumour where the sex incidence is approximately equal (Berg, 1950). The side of the body involved, in the present series, was 8 on the right side and 3 on the left.

The pathological status of these tumours is of importance, in particular, because of the difficulty and often impossibility in our present state of knowledge of effective treatment.

There are, in the literature to the time of writing, only 4 cases of jugular body tumour

in which metastases are postulated. In one case tissue resembling that of the original tumour was seen in a lymph node (Winship *et alii*, 1948); one case was stated to show multiple lymph node metastases (Bronzini, 1929); Lattes and Waltner (1949) reported and illustrated a case with a secondary deposit in the liver, closely resembling the primary growth; and Henson *et alii* (1953) reported multiple metastases in lungs, liver and spleen. Of these 4 cases, after careful assessment of the evidence presented, only the first and the third are acceptable. In that Bronzini's report has been reviewed only in retrospect the conclusion of a diagnosis (of such a rarity) is unjustified. In the case reported by Henson *et alii* the patient was a girl aged 17, who presented with a history of only a few weeks and died within three years with multiple widespread metastases. This last is most unusual and the histological diagnosis must be suspect. There is no reason to doubt, however, that malignant jugular and carotid body tumours occur (Romanski, 1954) but it is emphasized that such an event is rare. Apart from the 2 cases mentioned above (Winship *et alii*, 1948; Lattes and Waltner, 1949) there is no other record of metastasis in a case of jugular body tumour. Hence while the possibility of true malignancy can not be neglected, the occasional well-documented report of a malignant growth must not outweigh the evidence indicating that the great majority of the "tumours" of tissue belonging to the group of non-chromaffin paraganglia should be regarded as hyperplasias (Birrell, 1952, 1953).

The erosion of bone is sometimes accepted as an expression of malignancy but this occurs in many conditions which are not neoplastic, the bone resorption depending on physical characteristics independent of malignancy.

The nervous tissue found in these tumours appears to have undergone some distortion but not the degree of distortion produced either by inclusion in the tumour nor by the haphazard axon growth produced by infiltrating malignant cells damaging the nerve fibre.

Our knowledge of both the normal jugular body (another portion being described in this paper) and of the tumour is obviously incomplete; there is need in particular for further studies of the structure and behaviour of the tumour. Autopsy material, which is lacking, will doubtless become available in time. Treatment is a difficult problem which has evaded the combined efforts of the neurosurgeon and the otorhinolaryngologist and probably will ultimately depend upon more precise knowledge of the nature of the process involved.

SUMMARY

The normal jugular body is described. A new non-chromaffin paraganglion situated in the jugular ganglion of the vagus nerve is described and illustrated. It is suggested that all non-chromaffin paraganglia in this area be described under the term jugular body.

A series of 11 new jugular body tumours is recorded including 2 which were studied at autopsy. Clinical and radiological aspects are briefly considered.

In a patient presenting with a vascular polypoidal growth in the floor of the external ear together with radiological evidence of destruction of bone in the region of the petrous temporal bone, there is strong circumstantial evidence for the presence of a jugular body tumour, that is, a jugular body tumour syndrome.

Biopsy has been performed occasionally in this series and has been of some value but it is emphasized that it should be undertaken with an understanding of the risks involved.

The behaviour of the tumours, their resemblance to the normal body together with the finding of organized nervous tissue are all factors in regarding the tumours as hyperplastic in character. Inimical effects of the tumours are, in practically all cases, a function of their site of origin and not due to a malignant development.

No definite treatment has emerged, though ligation of the external carotid artery may be valuable, particularly in association with radiotherapy.

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CALCIFIED EPITHELIOMA OF MALHERBE

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IN 1880 Malherbe and Chenantais described a circumscribed lesion of the skin with a pronounced tendency to necrosis and calcification and named it "calcified epithelioma." Subsequent reports have firmly established the general features of the condition but conflicting opinions have been expressed regarding certain details of its structure as well as its site and mode of origin.

Search of material available in Melbourne revealed 25 cases and the clinical and pathological features of these form the basis of this paper. A brief survey of the literature is made, comparisons are drawn with previously recorded cases, and the origin and nature of the condition is discussed.

Historical note

Following Malherbe's and Chenantais's (1880) original description, a number of cases was reported in both French and German journals in the next thirty years, and a considerable literature as to the nature of the condition was built up. Despite isolated case reports by Eve (1882), Hutchinson (1890) and Nicholson (1916), no report of a series of cases nor a comprehensive account of the condition appeared in English until Ch'in described 10 cases from Peking in 1933. He also collected 116 previous recorded cases and reviewed the literature to that date. Cote, of Leeds, reported a further 12 cases in 1936 and several subsequent American series have been published. (Highman and Ogden, 1944; King, 1947; Lever and Griesemer, 1949).

Standard textbooks of pathology contain little or no account of the lesion but it is briefly mentioned by Willis (1953). No previous case has been reported from Australia.

Clinical and Pathological Material

The cases recorded in this paper were found by a search of the routine biopsy material of the Departments of Pathology of the University of Melbourne, the Royal Melbourne, Alfred and Prince Henry's Hospitals, Melbourne, for the past twelve years, all cases diagnosed as either calcified epithelioma or epidermal cyst with calcification being examined. Difficulties of classification rendered a more extensive search impracticable. In addition, material was supplied by several pathologists in private practice.

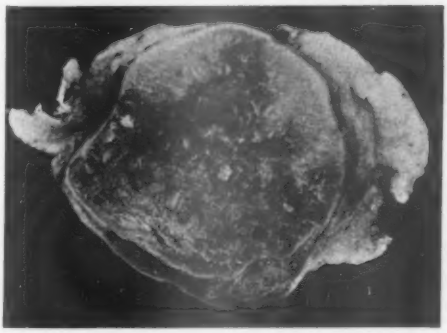

FIG. I. Photograph of a calcified epithelioma showing an intact epidermis overlying a well-defined and encapsulated lesion which has a cheesy appearance of the cut surface. (x 3)

Twenty-five cases conforming to the accepted description of calcified epithelioma were found and these form the basis of this report. The clinical and pathological details of these cases are summarized in the Table.

The method of collection of material precludes any accurate estimation of the incidence of the condition, but it is apparent that many more cases have been diagnosed in the last two years—10 appearing in this period. This makes it almost certain that earlier cases have been overlooked, and suggests that this condition occurs quite commonly in Melbourne.

General Features

Age incidence

The age of the patients ranges from 6-80 years, so the lesion may occur at any period of life. However, of the 22 cases in which the age is known, 5 are 21 years or less and

only 5 over 50 years. Ch'in (1933) reported 5 of 10 cases under 20 years of age, and Cote (1936) 8 of 12 aged less than 30 years. Thus the majority of cases occur in the first three decades; that is to say, at a much younger age than the common epithelial neoplasms of the skin.

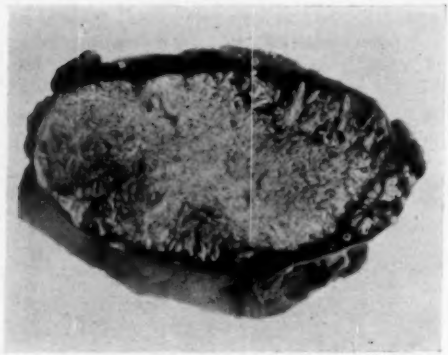

FIG. II. Photograph of a well-defined encapsulated calcified epithelioma with much granular calcified material in the cut surface. (x 2)

Sex incidence

In 23 cases where the sex is known there are 9 females and 14 males. This agrees with previous authors who have found no significant difference in the incidence of this condition between the sexes.

Trauma

In no case was a definite history of precedent trauma obtained. This confirms experience of other observers, but occasional cases appear to follow directly on local trauma. King (1947) reports such a case following a shrapnel wound of the forehead.

Signs and symptoms

All but one case presented as a lump lying beneath an intact skin, and present for a period ranging from 3 months to several years. In a number of cases the lump had recently increased in size but in no case was such increase described as rapid. The majority was diagnosed as sebaceous cysts. In one case *calcinosis cutis* was suspected and in another calcification was detected by X-ray examination. One case was thought to be an enlarged cervical lymph node. In one case the presenting symptom was a discharging sinus on the chest wall for twelve months. A localized swelling was palpable beneath the sinus. This case differed histologically from the rest and is separately described below.

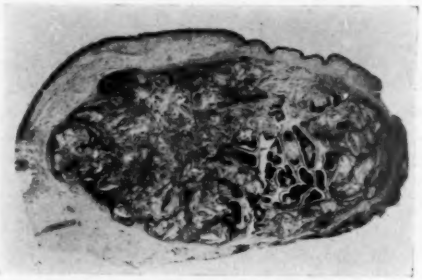

FIG. III. Photomicrograph of a section of a calcified epithelioma. Note the encapsulated nature of the lesion and the darkly-staining area of living epithelium in its interior. No lining squamous epithelium is present; cf Fig. IV. (x 10)

Site of lesion

Of cases where the site is known 9 occurred on the face and scalp, 5 in the upper limb, 5 in the lower limb and 4 on the trunk. In 2 cases 2 lesions were present, and in one several occurred on the scalp. Ch'in (1933) analyzing 116 cases found 57 occurred on face or scalp, with the limbs the next most frequent site.

Treatment and subsequent course

All cases were treated by local excision of the lesion. One recurred locally after four months requiring further excision, and the patient has since remained well for three years. In all other cases the treatment must be presumed effective. No complete follow-up is available but none of the patients has returned to a teaching hospital for further treatment, and except for the case mentioned above, no pathologist questioned can recall examining a recurrent lesion of this nature.

Macroscopic appearance

All the lesions studied form round or oval masses embedded in the dermis and subcutaneous tissues, and in all but one, where a narrow sinus communicates with the surface, the overlying epidermis is intact and normal in appearance. The lesions range in diameter from 0.5 to 4 cm. and all show clear demarcation from the surrounding tissues.

The consistence varies from firm to hard but all specimens cut readily with a knife. The cut surface varies from white to greyish yellow in colour and has a dry granular and sometimes "cheesy" appearance. In some cases small white flakes of calcified material are visible, and these may cause a gritting sensation when the lesion is cut.

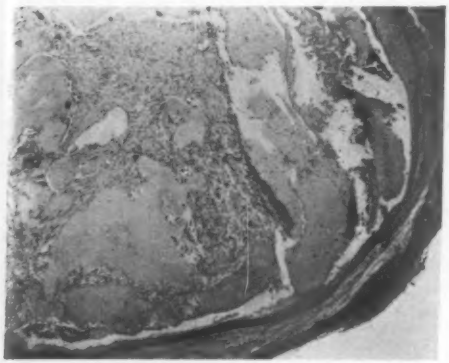

FIG. IV. Photomicrograph of portion of a section of a calcified epithelioma. A well-developed lining of stratified squamous epithelium is present enclosing masses of "mummified" epithelium which lie in a loose cellular stroma. Normal epidermis covers the lesion. (x 45)

Histological structure

All the lesions studied possess a similar basic structure but the several elements of which they are composed show a wide range of variation from one case to another. It is convenient, therefore, to describe first a typical lesion, and then discuss its component parts in more detail.

The typical lesion forms a roughly oval mass lying in the dermis and subdermal tissues beneath, and separate from an epidermis of normal appearance. The lesion is enclosed by a distinct fibrous capsule, lined internally by stratified squamous epithelium over part of its circumference. The interior is composed of irregular trabeculae of epithelial cells separated by a cellular stroma containing many foreign body giant cells. A proportion of the epithelial cells are necrotic and in the necrotic areas the cell outlines are clearly preserved and the nuclei still visible, forming so-called "mummified epithelium." Calcification in the form of fine dispersed granules or larger irregular plaques is present in the necrotic epithelium. Ossification may be seen in areas of heavy calcification.

(1) Capsule and stroma

The capsule is composed of dense fibrous tissue. In the majority it completely surrounds the lesion, but in 2 cases epithelial elements lie outside the main mass of the lesion. The stroma passes inwards from the capsule as irregular trabeculae separating the epithelial elements. It is much more cellular and loosely arranged than the capsule, the components being chiefly large and small mononuclear cells. In all but two of the cases with a definite stroma, foreign body giant cells are present and, in some, are very prominent and numerous. They occur more frequently near "mummified epithelium" than in the vicinity of "viable basiphil epithelium." Spaces, left by cholesterol crystals dissolved during preparation of the section, are seen near the giant cells in some cases. In one case no significant stroma is present (Case 9). Here two small lesions occur adjacent to one another: one is typical in all respects and the other shows all the usual epithelial elements but has no stroma. This probably represents an early stage in the development of this condition.

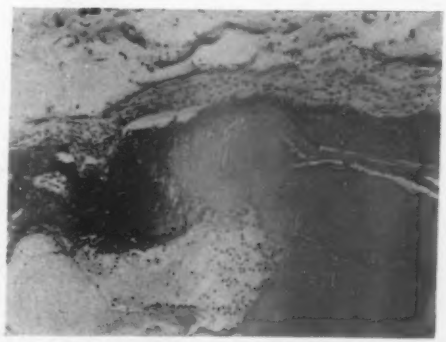

FIG. V. Photomicrograph of portion of a section of a calcified epithelioma showing stratified squamous, basiphil and "mummified" epithelium adjacent to each other. (x 90)

(2) Epithelium

This forms the major portion of all lesions and three distinct types may be seen.

(a) Mummified epithelium

This is present in all cases. It is entirely necrotic and forms irregular eosinophil

masses in which the outlines of squamous cells, and sometimes their nuclei, are clearly visible. In some areas cell outlines are less well peserved with the formation of pink amorphous material and in other areas, "pearl" formation similar to that of squamous cell carcinoma but composed entirely of dead cells, is seen.

In 8 cases this mummified material is the only epithelial element present in the lesion. These cases are the final "burnt-out" stage in the life history of this condition.

(b) Basiphil masses

These are present in 15 cases. These cells are clearly viable and mitotic figures are readily found in 5 cases. The cells are small, more or less rounded, and closely packed together so that, in some areas which present almost a syncytial appearance, cell boundaries are not easily seen. The cytoplasm is strongly basiphilic.

These cells are for the most part arranged in irregular bands around the necrotic masses, forming deeply-staining irregular papillae which stand out clearly from their pink-staining surroundings. In some cases separate masses of basiphil cells are present.

Clear transition is often seen between these cells and those forming the mummified masses. In the process the cell outlines become more distinct, the cell gradually assumes a squamoid form, the nucleus shrinks and may disappear, and the cytoplasm becomes progressively more oxyphil.

(c) Stratified squamous epithelium

This is present as a lining to the capsule in 6 cases. In 2 cases the lining is complete but in the others it occupies only a portion of the circumference. It consists of several layers of cells and transition from closely packed basal cells to more squamous superficial layers, such as occurs in normal epidermis, is apparent.

In 2 cases clear transition is visible between this lining epithelium and adjacent masses of basiphil epithelium.

(3) Calcification and ossification

Some degree of calcification is present in 20 cases. It occurs in the mummified epithelium and varies in amount from a dusting of fine basiphilic particles to the formation of heavy, densely basiphilic plaques. There is no obvious relation between the amount of necrotic epithelium and of calcification in any one lesion.

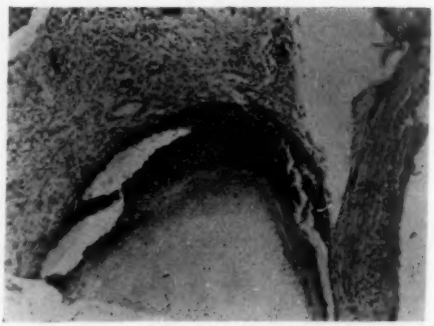

FIG. VI. Photomicrograph of portion of a section of a calcified epithelioma showing transition between basiphil and "mummied" epithelium. (x 90)

Ossification is present in one case only, a small lesion composed chiefly of irregular trabeculae of heavily calcified material with small areas of uncalcified epithelium, both mummified and basiphil. Some of the calcified trabeculae are partly replaced by well-formed bone in which osteoblasts are clearly visible. There is no suggestion of a marrow cavity nor have any myeloid elements been found.

(4) Melanin

Small amounts of melanin are present in 7 cases and pigment occurs in larger quantities in one case. It is in both living basiphil epithelium and mummified masses and may also be seen in phagocytic cells of the stroma. In no case is its amount sufficient to impart a brown colour to the macroscopic specimen.

One case (Case 25) differs so much from the remainder as to require separate description. This lesion is shown in Fig. X. The overlying normal epidermis is deeply invaginated into the underlying tissues to enclose a small tumour, portion of which consists of irregular trabeculae of small deeply-staining

epithelial cells and the remainder of masses of typical mummified epithelium. A scanty stroma lies between the epithelial elements. There is active inflammation in the neighbouring subepidermal tissues and many foreign body giant cells are present.

It is possible that this lesion began in a similar form to the remainder and that the surface communication is secondary but its appearance suggests rather that it is a primary tumour, growing down from the surface epithelium with secondary necrosis and mummification of much of its epithelium.

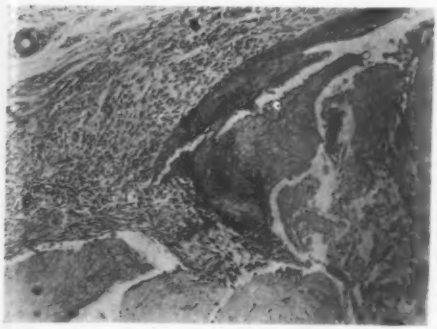

FIG. VII. Photomicrograph of portion of a section of a calcified epithelioma showing close relationship of stratified squamous, basiphil and "mummified" epithelioma. Only a small area of basiphil epithelium is present. (x 90)

ORIGIN AND NATURE OF THE LESION

In his paper of 1880 Malherbe suggested this condition arose from the abnormal proliferation of the lining of a sebaceous cyst. Some subsequent authors have agreed with him but numerous other hypotheses as to its origin have been advanced. The earlier ones are well reviewed by Ch'in (1933) who found that calcified epithelioma had been regarded as an endothelioma, a squamous cell carcinoma, a basal cell carcinoma, the derivative of an epithelial "rest," a traumatic epithelial inclusion, a cholesteatoma and a dermoid or epidermoid cyst.

It is not proposed to review these earlier theories again, but as the subsequent literature shows that considerable divergence of opinion still exists, the more recent theories will be briefly examined in an attempt to discover the reasons for this continued disagreement.

Cote (1936) marshalled strong evidence in favour of their origin from an epidermoid cyst and demonstrated portion of the epithelial lining of the presumed cyst in 7 of 12 cases. Despite this he rejected this hypothesis in favour of "a lesion *sui generis*, derived possibly from a sebaceous gland anlage, in which the final growth occupies an intermediate position between the ordinary epidermoid cyst and a carcinoma of basal cell type." His reasons for so doing were the appearance of the basiphil epithelium with plentiful mitoses, the progressive growth, the occasional recurrence after excision and the presence of some features of calcified epithelioma (encapsulation and foreign body giant cell reaction) in an undoubted *carcinoma sebaceum*. Only the first two of these objections have any substance. Recurrence after excision is a common occurrence in simple epidermoid cysts—due presumably to incomplete removal, and encapsulation and foreign body giant cell reaction are in no way specific of calcified epithelioma; in fact giant cell reaction is a prominent feature of most inflammations of epidermoid cysts and is probably due to difficulty of absorption, that is a specific physico-chemical state of their contents.

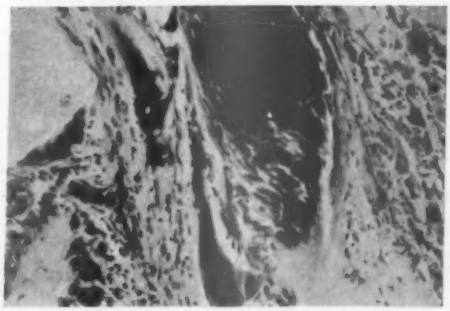

FIG. VIII. Photomicrograph of portion of a section of a calcified epithelioma showing heavy calcification in an area of "mummified" epithelium. Foreign body giant cells are prominent in the surrounding stroma. (x 180)

Turhan and Krainer (1942) and Highman and Ogden (1944) ascribed the origin of at least some cases to hair follicles. The evidence for this is the resemblance of the "basiphil" cells to cells of the hair bulbs and

the presence of melanin in 3 of 11 cases. This second reason is of no substance. As Stewart and Bonser (1948) and Birrell (1952) have shown, melanin, often in large quantity, may on occasion be present in any type of epidermal cell, and thus its presence has no localizing or developmental significance. A lining of stratified squamous epithelium is not described by these authors.

King (1947) divides the lesions into two classes—calcified epithelioma and calcified epithelial cyst. Of his 8 cases of calcified epithelial cyst only 2 "transitional cases" had any living epithelium — an incomplete squamous lining — and the single case he regards as calcified epithelioma is the only one to show the typical basiphil epithelium. It is the nature of this epithelium that leads him to separate this lesion from the rest. It is important to notice that this lesion also contains squamous epithelium, and in Fig. IV of his paper, transition from squamous to basiphil epithelium is clearly seen. King does not comment on this point.

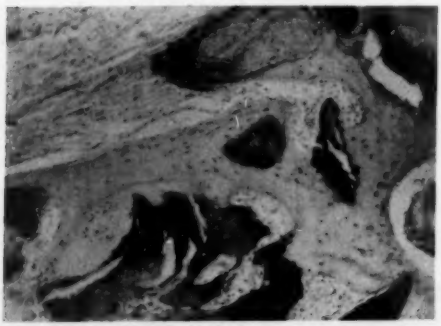

FIG. IX. Photomicrograph of portion of a section of a calcified epithelioma showing well-developed bone adjacent to clumps of basiphil epithelium. (x 90)

Lever and Griesemer (1949) follow King in dividing the lesions into calcified epithelioma and calcified epithelial cyst. They regard the essential difference as being the presence of basiphil epithelium and squamous epithelium respectively. The former class they regard as abnormal hair formation and follow King in using the occasional presence of melanin to support this origin.

This review of the recent literature shows that the difference of opinion is on three main points:

(i) the nature of the basiphil epithelium;

(ii) whether any or all the lesions are neoplastic or merely proliferations in simple cysts;

(iii) whether one or two lesions are included under calcified epithelioma.

In regard to the first point, study of this series has led to the following conclusions:

(1) Transition between basiphil cells and mummified epithelium is common. This transition has been noted by several previous authors and is clearly described and illustrated by Ch'in.

(2) The lining stratified squamous epithelium may be in direct continuity with basiphil masses, with clear transition visible between one cell type and the other. This is seen in 3 cases of the present series (Figs. V and VII). This relation has escaped comment by previous authors but basiphil-squamous transition is clearly illustrated in Fig. IV of King's paper.

Thus, at least in some cases, "basiphil" cells arise from squamous epithelium and in turn change into mummified squamous cells. Although properly termed basiphil from their staining reactions they are clearly dissimilar in behaviour from the basal cells of normal epidermis and should not be termed basal cells. Their similarity in appearance to the cells of basal cell carcinoma is undoubted; this only means that both are proliferations of the same epithelium and resemble one another in those regions showing no special differentiation, but may be distinguished clearly by the differentiated areas. Such resemblance implies no necessary relationship between the two lesions.

The second hypothesis, that basiphil cells are ill-developed hair bulbs (Highman and Ogden, 1944) rests solely on their supposed similarity in appearance, as the only other evidence adduced—the presence of melanin in some cases—is of no value in this regard. In the present author's opinion neither the living nor dead epithelium in calcified epitheliomas bears a real resemblance to any stage of normal hair formation.

The second disputed point—whether these lesions are neoplasms, is less easy to determine. There is no doubt that clinically the condition is benign. The occasional local recurrence must be regarded as due to incomplete removal and seems to occur no more commonly than in the treatment of simple epidermoid cysts. The literature contains no record of a calcified epithelioma exhibiting destructive local invasion or metastasis. There are obvious resemblances to epidermoid cysts in general form, encapsulation, location in the subcutaneous tissue, distribution over the body and in the occasional occurrence of multiple lesions. In addition local trauma sometimes precedes the appearance of either, and finally the epithelial lining of the presumed precedent cyst may be demonstrated in some cases of calcified epithelioma, with clear transition between this lining and the "basiphil" epithelium.

There is no feature, of at least the great majority of these lesions, inconsistent with their being simply an hyperplasia of the lining of a epidermoid cyst with later degeneration which may lead to death of all the epithelial elements. Willis (1953) inclines to this view of the condition. The causes of the hyperplasia and subsequent degeneration are completely unknown.

FIG. X. Photomicrograph of a section of a calcified epithelicma (Case 25). A small tumour is invaginated from the skin surface. Portion of the tumour shows papillae of basiphil epithelium and the remainder consists of "mummified" epithelium. (x 6)

If this hyperplasia and degeneration be accepted as the origin of most cases, the final problem is whether it applies to all. Distinctions between calcified epithelioma and calcified epithelial cyst drawn by King (1947) and Lever and Griesemer (1949) are not acceptable for reasons already discussed; but so long as the cause and nature of the peculiar "mummified" degeneration of epithelium — the one feature common to all stages of the life cycle of these lesions—remains unknown, the possibility exists that such a change may occur in the epithelium of a neoplasm.

In one case (Case 25) of the present series this would appear to explain the origin of the lesion best. A similar appearance cannot be found in the literature, and the effect of such degeneration on the subsequent cause of the tumour is unknown. One of Gromiko's (1927) cases may come into this category; the tumour recurred twice after removal but then reached the size of a foetal head and amputation of the arm was finally performed. This tumour was in many respects atypical—showing rapid growth and much haemorrhage into its substance—but undoubted bone formation was present, together with active and mummified epithelial elements. If accepted as a calcified epithelioma it is the only recorded case that is beyond doubt neoplastic.

The other prominent features of these lesions — calcification, ossification and the foreign body giant cell reaction in the stroma —are of little importance in determining their nature. Calcification is clearly a secondary phenomenon consequent to degeneration of the epithelium. It is not seen in the absence of such degeneration which, however, occurs commonly without calcification. Ossification seen only once in this series, follows calcification. As Ch'in (1933) points out and clearly illustrates, it occurs in the calcified degenerate epithelial masses and not primarily in the stroma as some authors have claimed.

No more is known of the mechanism of this calcification and ossification than of similar depositions in degenerate material in other conditions, but here as elsewhere lipoid deposition is a common precedent factor. By special stains Ch'in demonstrated large amounts of lipoid in the degenerate epithelium, and characteristic cholesterol spaces are visible in several cases of this series although special staining was not used. These lipoids may account, in part, for the prominence of foreign body giant cells in the stroma.

TABLE 1

THIS GIVES THE GENERAL FEATURES OF THE GROUP OF CASES STUDIED

Case Number	Age in Years	Sex	Location of Lesion	Known Duration prior to Excision	Diameter in Centimetres	Capsule	Epithelium						Stroma			Calcification	Ossification	Melanin			Remarks
							Squamous Lining	Basiphil	"Mummified"	Mitoses in Basiphil	Transition Squamous to Basiphil	Transition Basiphil to "Mummified"	Amount	Type	Foreign Body Giant Cells			Living Epithelium	"Mummified" Epithelium	Stroma	
1	80	F	Scalp	Many years	4·0	C	C	?	++	++	+	+	+	Loose	Few	Slight	–	–	–	–	One of multiple scalp lesions—transition lining squamous to "mummified" epithelium with no clear basiphil stage
2	—	—	—	—	3·0	C	—	–	++	–	–	–	++	Loose	++	Much fine dust	–	–	–	–	No history obtainable
3	—	—	—	—	3·0	C	–	++	++	–	–	+	++	Loose	++	Heavy masses	–	–	–	–	No history obtainable
4	21	M	Thigh	18 months	2·5	C	–	+	++	–	–	–	+	Loose	Few	Heavy masses	–	–	–	–	
5	30	M	Leg	Many years	1·0	IC	–	+	+	–	–	+	++	Dense	+	Very heavy	+	–	+	+	Surface ulceration for 12 months prior to excision—only case in which ossification is present
6	47	M	Forearm	4 years	1·5	–	—	–	++	–	–	–	+	Dense	–	–	–	–	–	–	No living epithelium present
7	59	M	Scapular region	—	2·0	IC	–	+	++	–	–	+	++	Loose	++	–	–	–	+	+	
8	13	F	Arm	3 months	2·0	C	–	+	++	–	–	+	+	Loose	+	Heavy masses	–	–	–	–	
9	66	M	Cheek	3 months	1·0	C	Almost C	+	+	++	+	+	+	Loose	+	Fine dust	–	–	–	–	Two small adjacent lesions—one with and one without stroma
10	68	M	Buttock	—	7·0	IC	–	–	++	–	–	–	+	Loose	+	Fine dust	–	–	+	–	No living epithelium present
11	9	F	Neck	Few months	2·0	IC	IC	++	+	++	–	+	+	Loose	+	Fine dust	–	+	–	–	High proportion of living epithelium—recurred 4 months after first excision
12	50	F	Back	3 months	2·5	C	C	?	++	–	+	+	+	Loose	+	–	–	–	–	–	Similar to Case 1—no distinct basiphil epithelium
13	—	M	Arm	—	2·0	IC	IC	+	+	+	+	+	++	Loose	+	Slight	–	–	–	–	Clear transition squamous to basiphil to "mummified" epithelium

Case Number	Age in Years	Sex	Location of Lesion	Known Duration prior to Excision	Diameter in Centimetres	Capsule	Epithelium						Stroma			Calcification	Ossification	Melanin			Remarks
							Squamous Lining	Basiphil	"Mummified"	Miloses in Basiphil	Transition Squamous to Basiphil	Transition Basiphil to "Mummified"	Amount	Type	Foreign Body Giant Cells			Living Epithelium	"Mummified" Epithelium	Stroma	
14	50	M	Eyebrow	6 months	1·0	IC	–	++	++	–	–	+	++	Loose	++	–	–	–	–	–	
15	33	M	Leg	—	2·5	–	–	++	+	–	–	?	+	Fibrous	+	Fine dust and heavy masses	–	++	+	+	Fragmented section—abundant melanin in epithelium and stroma
16	27	F	Face	12 months	1·0	C	–	–	++	–	–	–	+	Fibrous	+	Heavy masses	–	–	–	–	No living epithelium
17	33	M	Shoulder	—	3·0	C	–	–	++	–	–	–	+	Loose	++	Heavy masses	–	–	–	–	No living epithelium—second lesion present on arm—clinical diagnosis *calcinosis cutis*
18	14	F	Arm	Few years	1·0	C	–	–	++	–	–	–	+	Fibrous	+	Fine dust	–	–	–	–	No living epithelium
19	33	M	Knee	9 months	1·0	IC	–	–	++	–	–	–	+	Fibrous	+	Heavy masses	–	–	–	+	No living epithelium—calcification seen in X-ray of leg
20	41	F	Scapular region	7 months	4·0	–	–	++	++	+	–	+	+	Loose	++	Heavy masses	–	–	–	–	Fragmented section
21	10	F	Face	12 months	1·0	IC	IC	+	++	–	+	+	++	Loose	++	Fine dust	–	–	–	–	Deeper part of section fragmented
22	6	M	Glabella	Few months	1·0	C	–	–	+	–	–	–	+	Fibrous	–	Heavy masses	–	–	–	–	Calcified masses form bulk of lesion
23	30	M	Temporal region	—	1·0	C	–	+	++	–	–	+	++	Loose	++	Heavy masses	–	+	–	+	
24	38	M	Scalp	24 months	2·5	–	–	+	++	–	–	+	+	Loose	+	Heavy masses	–	+	+	+	Fragmented section
25	59	F	Anterior chest wall	12 months	1·5	C	–	+	++	–	–	+	+	Loose	–	–	–	–	–	–	See text—? different type from other lesions

C = Complete. IC = Incomplete.

Although these lesions are believed by some to be derived from simple epidermoid cysts, they should be clearly distinguished from simple calcification of such a cyst. Here the characteristic epithelial elements, both living and dead, are absent and the cyst contains only structureless keratin in which the deposition of calcium salts occur. A lining of stratified squamous epithelium is often present. Such cysts are well described by Warvi and Gates (1943) and 4 typical examples were found whilst collecting this series.

The final problem is that of the nomenclature of these lesions. The use of the term "epithelioma" is open to the double objection that the condition in most cases is not a neoplasm at all and if it were, epithelioma gives no real description of the lesion. King's (1947) suggestion "mummified epidermal cyst" lays emphasis on the most characteristic feature of the lesion and stresses its non-neoplastic character. It is the logical name for this condition, but the older title has persisted in papers subsequent to King's, and appears too firmly associated with the condition for a sudden change to be successfully made. However, the addition of the name of the man who first described it serves to distinguish it from lesions with which it has been confused in the past. Thus the title used in this paper—Calcified Epithelioma of Malherbe.

SUMMARY

1. The recent literature concerning calcified epithelioma is reviewed.
2. The clinical and pathological features of 25 new cases are recorded. Though these are the first cases recorded in Australia, the condition is not uncommon in Melbourne.
3. The lesions are clinically benign and adequate local excision is the logical treatment.
4. Almost all the lesions are epithelial hyperplasias in association with epidermoid cysts with secondary degeneration of the hyperplastic epithelium, that is to say, they are not neoplasms.
5. One case is described in which the epithelial degeneration characteristic of calcified epithelioma occurs in a benign skin neoplasm.
6. The nomenclature of the lesion is briefly discussed.

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TREPHINE ("DRILL") BIOPSY IN TUMOUR DIAGNOSIS

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Introduction

THE histological diagnosis of a tumour in modern clinical practice is of paramount importance, and the assertion of Ellis (1947 that "histology is still the touchstone of cancer work," although universally respected by the morbid anatomist, is unfortunately, and not infrequently, given only lip service by the clinician.

The modern treatment of malignant disease is by no means standardized, and the conflicting views which have arisen from statistical, pathological and clinical studies, can only be resolved by adopting a more critical analysis of the material and methods used. It is abundantly clear that the veracity of the results of treatment, particularly curative results, can only be determined by means of accurate diagnosis and classification. In this respect, establishment of a histological diagnosis prior to the institution of treatment, is of overwhelming importance, and any procedure which facilitates our means of determining the pathological histology of a malignant lesion, with accuracy, safety and utility, is worthy of the closest attention. This article presents an attempt by the writer to evaluate the operation of trephine ("drill") biopsy in tumour diagnosis and is based on initial personal experiences of its use.

Biopsy of Neoplasms — Usefulness and Dangers

The treatment of neoplastic disease attempts three essential objectives:—

(i) Curative.

(ii) Prolongation of life beyond expectation for the particular neoplasm.

(iii) Palliative.

It is obvious that an assessment of the results of treatment as regards cure and prolongation (or shortening) of life in malignant disease, implies a keen appreciation of the behaviour and natural history of untreated neoplasms. Unfortunately, our knowledge in this respect leaves much to be desired, and although attempts at correlation of the survival rate for different types of untreated malignancy have been made (Lazarus-Barlow and Leeming, 1924; Greenwood, 1926; Nathanson and Welsh, 1936, 1937a, 1937b; Shimkin, 1951), the criteria used in the classification are too broad to aid the clinician in assessing the results of therapy in a given case of malignant disease. Such statistics largely fail to particularize behaviour as regards the age of the patient (excepting Greenwood, 1926), histological type and rate of growth of the tumour and the cause of death (viz., whether due to local manifestations of the primary growth or metastases). The latter consideration is of the utmost importance in cancer treatment, and it is becoming apparent, that whilst the surgeon and radiotherapist have much to offer in the local control and eradication of the primary tumour, radical attempts to encompass metastatic manifestations of the growth are usually futile and ill-conceived (Weyde, 1947). Furthermore, evidence is accumulating, that the removal of a primary tumour in the presence of widespread metastases, whether manifest or cryptic, can often lead to a generalized progression of tumour deposits, resulting in a shortened life span, and defeating one of the objects of treatment. Although the pathological histology of a neoplasm is not a *sine qua non* in this respect, it is still the single most important diagnostic measure we possess in determining the behaviour of a given neoplasm, and the necessity and the usefulness of biopsy is self-evident.

The obvious confusion and lack of unanimity of opinion in regard to the dangers of biopsy of malignant neoplasms is understandable, when the problem is viewed as follows:—

(i) General deficiencies in our knowledge of the pathology of neoplasms.

(ii) Difficulties in obtaining experimental evidence as to the effects of biopsy on the progress of neoplasms, and particularly in relating such evidence to the human subject.

(iii) Fallacies in relying on clinical impressions — often based on material insufficient to allow statistical evaluation, and entirely devoid of scientific control and standardization.

(iv) Non-specification of such dangers in relation to the various types of biopsy, and subsequent methods of treatment.

It is not proposed to make a comprehensive review of this question, which has been done elsewhere (Ackerman and Regato, 1947; Maun and Dunning, 1946; Kaae, 1952).

However, certain aspects will be considered.

(i) *Induction of remote metastases*

Many clinicians of wide experience are convinced that biopsy of neoplasms is fraught with the danger of inducing both blood born emboli and lymphatic dissemination. Thus, Ogilvie (1951) writes:—

> ". . . in my opinion biopsy is often a device for postponing decision and shelving responsibility, a refuge for the incompetent and a moral support for the timid; it is an added danger to the patient and seldom necessary to the surgeon who knows his job . . . . Were biopsy to be made a penal offence, very few people would suffer, and countless lives would be saved . . . . A large ulcer in the mouth is either cancer or it is not, and the surgeon who does not know should refer the case to a surgeon who does."

Unfortunately, the "surgeon who knows" is by no means infallible and difficulties encountered in the clinical diagnosis of certain tumours are obvious, for example, the lymphadenopathies and bone tumours; the management of such cases, without a histological study, seems unjustifiable. Furthermore, surgical intervention is not always in the best interests of the patient suffering from malignant disease, and other forms of treatment require a more subtle appreciation of the characteristics of a tumour. The dangers of biopsy, implied in the above statement, are entirely impressionistic, and have not been substantiated either experimentally or by statistical evaluation of adequately controlled series of cases. The following case histories demonstrate how easily a false impression may result from deductions based on individual examples.

Case 1

J.H., female, aged 13 years. When first seen on 11th September, 1952, this patient gave a history of pain and stiffness in the right lower leg following a fall eight months previous. On examination, there was a diffuse fixed swelling measuring 7 cm. x 7 cm. x 1 cm. situated in the outer aspect of the right lower leg, apparently arising from the fibula. A radiograph taken at the time (12th September) showed: "Partial destruction of the cortex of the middle one-third of the right fibula, with radiating spicules of bone producing a 'sun-ray' effect. Appearances favour osteogenic sarcoma. Chest — no metastases seen."

Two courses of radical X-ray therapy were given (a tumour dose of 5,400r in nine weeks finishing 20th November, 1952, and a further tumour dose of 3,900r in eight weeks finishing 6th April, 1953).

A radiograph of the chest taken on 2nd February, 1953, failed to reveal metastases, and at the time, excellent clinical and radiological resolution was taking place in the fibula, with "further bone condensation."

On 5th June, 1953, it was decided that a trephine biopsy of the lesion should be undertaken to establish a diagnosis, before recommending radical surgical treatment, by amputation. However, before the biopsy could be undertaken, conveniently, the patient reported for a further radiograph of the bony lesion and the chest (8th June, 1953). The report was: "Right fibula — no evidence of any active process. Chest — multiple round secondary deposits in both lungs."

In this case, had the biopsy been performed as arranged, how easy it would have been to attribute lung metastases to the biopsy procedure?

Case 2

R.B., male aged 68 years. Was first seen on 13th October, 1952. He had a tender soft swelling over the left ischial tuberosity, of some months' duration, diagnosed as an ischial bursitis by the surgeon, and ten days later a short course of deep X-ray therapy was commenced (tumour dose 600r in 12 days).

However, he did not get relief from the treatment, and when next seen on 24th February, 1953, the swelling was larger and the pain in the buttock severe.

On 24th February, 1953, I performed a trephine biopsy, and the pathologist reported: "Clumps of large polyhedral carcinoma cells. In parts there is some suggestion of an acinar pattern; elsewhere the carcinoma is hyalin and necrotic."

A rectal examination disclosed a mass obliterating the left lateral prostatic sulcus which was continuous with the ischial tumour. A blood serum acid phosphatase estimation was done and 14 King Armstrong units were present.

The patient's condition rapidly deteriorated and death took place on 13th May, 1953 (approximately nine months after the onset of his symptoms, and three months after the biopsy was performed).

A post-mortem examination revealed the presence of a carcinoma of the lung with metastases in the ischium. Bronchopneumonia was the cause of death.

By the time biopsy was performed in this case, the patient's condition was very poor. There was no post-mortem evidence of the precipitation of metastatic spread from the biopsy of the ischial lesion, and it is most unlikely that biopsy could in any way have jeopardised the patient, when death took place three months later with a terminal bronchopneumonia.

Case 3

A.S., female aged 70 years. Was first seen on 11th June, 1952, with a hard fixed tumour in the left breast, 4.5 cm. in diameter, and a hard mass in the left axilla, 6 cm. in diameter.

Next day a radiograph of the chest was performed and the film showed the presence of "multiple rounded metastases in both lungs."

At the time the patient's blood was examined and a haemoglobin of 94 per cent. and leucocytes numbering 10,000 per cmm. were reported. Stilboestrol by mouth was ordered.

In 18th June, 1952, I performed a routine trephine biopsy of the breast tumour. The report read: "Small groups of spheroidal cells forming irregular cords and tubules. Carcinoma of breast."

On that day it was noted in the clinical history that "In view of widespread condition, she is keeping remarkably well." However, the patient did not attend the clinic again, and enquiry revealed that she died on 20th July, 1952 (one month after the biopsy was performed).

The question arises, whether biopsy was a factor in shortening this patient's life. Whilst widespread metastases were present prior to biopsy, her clinical well-being at the time was noted and yet death took place within five weeks. Alhough it would seem that biopsy did play a part in causing a rapid termination of her illness, resulting in death, it is obvious that other factors could be equally incriminated in such a case, and no deductions can be made whatsoever.

Most writers, well versed in oncology, agree that biopsy *per se* does not induce remote dissemination (Cade, 1951; Ackerman and Regato, 1947; F. Ellis, 1947; Martin and E. B. Ellis, 1934). Thus Martin and Ellis (1934) write: "We believe that histological diagnosis is highly desirable in all and absolutely essential in the majority of suspected neoplasms, in order that proper therapeutic measures may be outlined."

Some authorities adopt a more cautious attitude. Aird (1949) writes: "In biopsy there is no danger of precipitating metastasis by mechanical disturbance"; and later, "The melanoma, the neurofibroma, the synovioma and the osteoclastoma are perhaps the only four tumours in which partial biopsy may precipitate malignant change."

An analysis of case series, with and without biopsy, largely has failed to substantitate the dangers of biopsy to the patient. Thus, there was no deleterious effect on the five-year cure rate for cancer of the cervix uteri (Marzloff, 1923), accessible cancer of the tongue and lip (Paterson and Nuttall, 1939), tumours of bone (Coley *et alii*, 1931), and cancer of the breast (Kaae, 1952).

Harrington (1935) reported a higher incidence of axillary metastases and poorer prognosis, when a "minor operation" had been performed prior to the institution of radical treatment in cancer of the breast, but failure to elucidate the nature of the procedure, the selection of cases and the time interval between the two interventions, invalidates any assumptions being made.

Similarly the higher incidence of local recurrences in groups submitted to biopsy, noted by Taylor and Wallace (1950), are too small for statistical analysis, although suggestive that some forms of biopsy may spread malignancy *(vide infra)*. A recent study of Nohrman (1949) indicates that in carcinoma of the breast a critical interval exists between biopsy and radical surgical treatment, which influences prognosis. However, his results need further confirmation.

On the experimental side, it has undoubtedly been shown that massage of tumours facilitates the manifestation of remote metastases (Tyzzer, 1913; Knox, 1922; Marsh, 1927). In carcinoma of the breast Engelbreth-Holm (1942), has shown that rough massage is apparently attended by an increase in tumour spread.

However, it is to be stressed that in such experiments, massage has only increased the number of manifest metastases and has not at

any time been shown to induce the power of metastatic potentialities in an erstwhile, non-metastasising tumour.

In this regard it is cogent to note that we have very little real knowledge as to the phase in the life history of a neoplasm when metastatic potentiality arises. It is ignorance in this respect which invalidates many assumptions, not only concerning the dangers of biopsy, but also the clinical staging of malignant tumours, the virtues of early diagnosis, and the absolute results of treatment.

It is becoming increasingly evident that such metastatic capabilities arise *de novo* with the genesis of many malignant growths, i.e., it is an inherent property of the tumour and certainly not to be regarded as either a biological accident or a consequence of trauma *per se*. In the case of biopsy performed by a sharp cutting instrument, induction of metastases is even less likely on *à priori* grounds.

Maun and Dunning (1946) have studied the effects of biopsy of malignant neoplasms in animals. Their experiments are reliable in so far as standardization of tumour, host and method of biopsy were attempted; relatively homogeneous inbred rats and identical tumour homotransplants were used for the experiments. They failed to show that a simple biopsy by a cutting instrument had any adverse effect on average survival time, or the percentage of metastases in a transplanted adenocarcinoma and a transplanted squamous cell carcinoma.

(ii) *Local spread*

Whilst local biopsy of ulcerating growths, performed by means of a scalpel, biopsy punch or curette, is harmless in this respect, the contention that "biopsy by surgical incision through normal tissues may be followed by serious complications in the more malignant growths" (Martin and Ellis, 1934), is undeniable, and must be the experience of most clinicians dealing with malignant conditions. Not only does the opening up of tissue planes frequently give rise to extensive local spread, particularly in such tumours as soft tissue sarcomata and anaplastic carcinomata, but fungation and wound dehiscence is of common occurrence in the open biopsy of infiltrating tumours, however careful the wound closure is made.

The desirability of a minimal disturbance of normal tissues overlying a tumour is obvious, and in this regard, needle and trephine biopsy approaches the ideal.

(iii) *Modification of the clinical setting*

It cannot be too strongly emphasized that any procedure which delays possible palliative or curative treatment in a case of inoperable cancer is to be condemned. Furthermore, any procedure which alters the clinical setting of the disease in such a way as to detract from the efficacy of such treatment, is also highly undesirable.

Open incisional biopsy is culpable in both respects. Submission to surgical principles demands an adequate exposure and a large wound, with the resultant delay in applying either external or interstitial irradiation treatments (still the mainstay in the treatment of inoperable cancer), and furthermore, always gives rise to some degree of interference with blood supply and scarring, both of which are of paramount importance in the sensitivity of a tissue to ionizing radiations, leading to a decrease in both radio-sensitivity and radio-curability.

Needle and trephine biopsy permits of immediate treatment and causes a minimal change in the nutrition of the tumour.

DEVELOPMENT OF ASPIRATION AND TREPHINE BIOPSY

As long ago as 1904 Grieg and Gray, in England, described aspiration biopsy of lymph nodes to obtain tissue fragments for diagnosis. However, the most extensive use of aspiration biopsy has been made in the United States, particularly at the Memorial Hospital, New York, where this procedure was adopted in 1926 (Martin and Ellis, 1930), and by 1934 had resulted in 1,400 positive cancer diagnoses through its use alone, the specimens being prepared by a smear technique and rapid fixation (Martin and Ellis, 1934). More recently F. Ellis (1947) has reported favourably on its use at the London Hospital and recorded the results in 689 aspiration biopsies made by using ordinary needles with a bayonet fitting.

In Australia, Wilson (1945) reported on the use of aspiration biopsy and made an extensive review of the literature to that date; Parsons, Garlick and Motteram (1948) reported on the use of aspiration biopsy in liver disease and recorded results in 144 cases studied in the Clinical Research Unit, Royal Melbourne Hospital.

However, the paucity of material obtained by aspiration biopsy, usually necessitating a smear technique, has led to considerable disrepute of the procedure. The pathologists have largely expressed dissatisfaction at being asked to report on fragmentary specimens, often distorted, and the clinician has recorded a considerable proportion of negative results. Thus, in the hands of F. Ellis (1947) the proportion of useful biopsies in a total of 689 cases was 63 per cent., whilst for bone tumours, Snyder and Coley (1945) recorded 67.5 per cent. useful results in 474 cases, of which 93 cases (19.6 per cent.) also required the procedure repeated.

Such results led to modifications in the type of needle used and aimed at providing better specimens. Franseen (1941) used a 14 gauge needle with three cutting teeth, which was manually rotated and designed to act as a cutting trephine and provide a core of tissue. This needle has been very successful in the hands of Parsons *et alii* (1948) for liver biopsy. Another needle which has received approbation is the Silverman pattern (Tenopyr and Silverman, 1941); this consists of an inner split 17 gauge needle to transfix the tumour, a central tissue core being "avulsed" by an outer 14 gauge needle acting as a collar to the inner needle.

In the hands of the writer, aspiration biopsy using both an ordinary bayonet tipped needle and the Franseen needle has been most unreliable, and two years ago was discontinued in favour of trephine biopsy.

The use of a rotating trephine was first described by Kirschner (1934) but owes its development to Christiansen of Copenhagen (1940, 1942). Since its introduction, Christiansen has used it extensively and in 1943 reported its use in over two thousand patients (Christiansen, 1943).

F. Ellis (1947) also reports favourably on its use in 218 cases in various sites. Kaae (1948) has published his results of trephine biopsy in tumours of the breast (284 cases). The present report is based on personal experience of over 300 trephine biopsies and this procedure has entirely changed the complexion of biopsy in the writer's opinion.

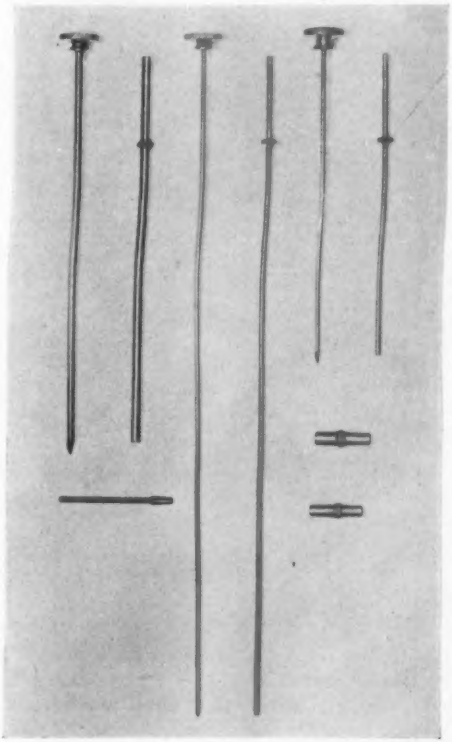

FIG I. Photograph of the trephines and applicators.

ARMAMENTARIUM IN TREPHINE BIOPSY

This has been described elsewhere (Christiansen, 1940; Ellis, 1947; Bond, 1951), and with a few modifications, set out below, the apparatus used in the present communication is similar.

(i) Trephines

These are of 1 mm. and 2 mm. internal diameter, and fitted with a central trocar, for insertion down to the tumour. The length of the needle shaft varies from 8 cm. to 16 cm. The needle end is squared off and

sharpened for use in soft tissue tumours. For biopsy of bone, where cortex is relatively intact, it was found that a sharpened serrated end was much more satisfactory (see Fig. I).

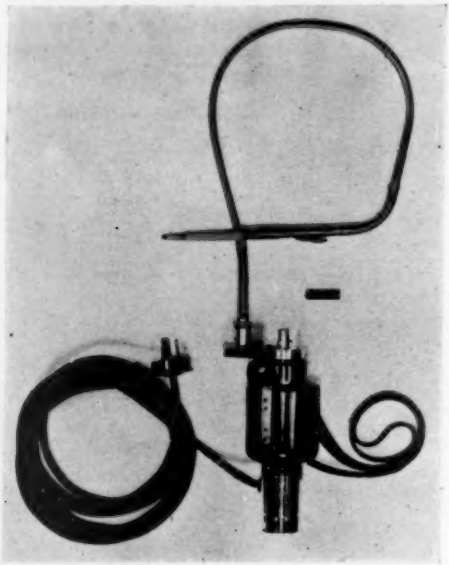

FIG. II. Photograph of the Bosch-Naylor portable motor, flexible drive and drill chuck.

(ii) Method of rotation

An electric portable dental drill is used to rotate the trephine. The appartus used by the writer is a standard miniature portable motor made by Bosch-Naylor, wired for both direct current and alternating current and geared to give two speeds of 3,000 and 6,000 revolutions per minute (Fig. II). A flexible cable arm and hand piece are attached to the head, and a hand operated switch is also fitted to the motor. Although the chuck will accommodate the trephine shaft, it was found necessary to use an inter-connecting shaft and applicator for the trephine to prevent the blood from vascular tumours entering the chuck mechanism. The same applicator will take the fitting of a record syringe to enable negative pressure to be applied to the tissue core on removal from the tumour.

In the apparatus described by Bond (1951), a portable 1/18 horse-power motor is used to give a trephine speed, varying from 600 to 3,500 revolutions per minute. This apparatus has the advantage of enabling control of speed by means of finger pressure on the chuck, and the operating switch is also fitted to the chuck casing, and controlled by the operator.

In the experience of the writer, however, the higher speed of rotation (6,000 revolutions per minute) is a distinct advantage in removing a soft core of tissue, and eliminates all pressure and tension in the tumour.

For the removal of cylinders of hard bone, the power of the apparatus used is insufficient, and the writer uses a simple hand operated drill to rotate a toothed tipped trephine. This method was found to provide a beautiful undistorted specimen and has been extensively adopted in iliac crest biopsies for the study of marrow failure in blood dyscrasias.

TECHNIQUE

This has been adequately described by other authors (Christiansen, 1940; F. Ellis, 1947).

However, the following features need emphasis:—

(i) Only the overlying skin needs a minimal infiltration of local anaesthetic to enable a small stab (3 mm.) with a tenotome (a Bard Parker blade No. 11 is used). Under no circumstances is the tumour or its immediate surroundings infiltrated with local anaesthetic. Such a procedure is both unnecessary and undesirable for reasons already discussed.

(ii) The trephine with trocar *in situ*, is manually passed to the proximal limit of the tumour to enable the specimen to include some normal tissue, if possible, and make the pathologist's task easier and his report more informative in respect to the architecture of a lymph node in reticuloses, and infiltration into surrounding tissues for an invasive tumour.

(iii) It is found desirable to avoid traversing skeletal muscles, which can

undergo marked shortening, for example, the sternomastoid muscle in thyroid gland biopsy, owing to "gripping" of the trephine which occurs from direct stimulation of the muscle fibres. It is found that this difficulty can usually be easily overcome by proper selection of the point of entry and angle of direction of the trephine.

(iv) The tumour must be steadied by means of posture, or manipulation and manual pressure, prior to drilling. In the case of small, rather inaccessible lymph nodes, this presents the greatest difficulty and leads to some failures, particularly in trephine biopsy of small mobile nodes in the apex of the axilla.

(v) The soft tissue core is detached by negative pressure applied by a syringe containing normal saline and received into the barrel on withdrawal of trephine with syringe connected. For soft tumours, a minimal amount of negative pressure is desirable to prevent undue fragmentation of the core. In the case of tumours with a marked fibrous stroma, a higher negative pressure

TABLE 1

RESULTS TABULATED FOR FIRST 300 CONSECUTIVE CASES OF ROTATING TREPHINE BIOPSY

Site of Trephine Biopsy	Number of Cases	Useful Positive Results	Negative Results
Body Wall	4	4	0
Bones	67	64	3
Brain	1	1	0
Breast	44	43	1
Extremities	2	1	1
Lachrymal Gland	1	1	0
Liver	10	9	1
Lung	9	8	1
Lymph Nodes	124	112	12
Maxillary Antrum	11	10	1
Orbit	1	1	0
Palate	3	3	0
Parametrium	4	4	0
Parotid Gland	4	4	0
Pyriform Fossa	1	1	0
Tongue (Posterior Third)	1	1	0
Tonsil	6	6	0
Thyroid Gland	7	6	1
Total	300	279	21

The negative result in 21 cases includes failure to obtain representative or adequate material and all diagnoses, subsequently proven wrong.

A positive result in 279 out of 300 cases represents an accuracy of diagnosis in 93 per cent. of all cases, by means of trephine biopsy.

is required to ensure detachment of the core.

In obtaining bony cores, syringe suction is useless for removal; the base of the core is detached by slight alterations in the trephine angle and the core needs to be expressed by a stilette (often somewhat difficult in the case of long cores).

(vi) A single stitch is used to close the tiny incision — not to prevent "fungation" but to act as a haemostatic. It is removed in a few days.

RESULTS

The results in a personal series of the first 300 consecutive trephine biopsies are set out in Table 1 which gives the site of biopsy, correlated with the number of cases for each site and the number of positive and useless results. The latter includes failure to obtain sufficient material, failure to obtain representative material and diagnoses later proved wrong.

Table 2 sets out the number of trephine biopsies performed for the corresponding sites in bones, and Table 3 tabulates the sites for lymph nodes.

TABLE 2

Classification of lymph node biopsy according to anatomical grouping and showing number of cases in each group.

Anatomical Group of Lymph Nodes	Number of Cases
Axillary	31
Cervical	67
External Iliac	5
Inguinal	13
Internal Mammary	2
Pre-auricular	5
Supratrochlear	1
Total	124

TABLE 3

Showing distribution of the trephine biopsies of bones performed according to skeletal site (excluding maxilla, 11 cases, included in Table 1 as "Maxillary Antrum").

Bone on which Trephine Biopsy Performed	Number of Cases
Clavicle	2
Femur	11
Humerus	6
Mandible	1
Mastoid	1
Os Coxae	22
Ribs	2
Sacrum	8
Scapula	4
Sternum	7
Vertebrae	1
Zygoma	2
Total	67

An overall useful result of 93 per cent. is recorded for all trephine biopsies in this series.

COMPLICATIONS AND CONTRA-INDICATIONS

The present series is too recent and too small to enable an opinion as to whether trephine biopsy enhances or induces metastatic manifestations of a malignant growth.

However, in no case was there any evidence of precipitation of rapid deterioration in the patient's condition or radiological and other signs of precipitating metastases.

Locally, the main complication has been the occasional puncture of vessels in the neighbourhood of the tumour. On one occasion the subclavian artery was traversed by the trephine, but digital pressure for a few minutes controlled the bleeding and there were no after effects. Ellis (1947) has recorded a similar example. Puncture of large veins and biopsy of highly vascular tumours (particularly of bone and thyroid)

has on a few occasions led to marked venous bleeding, but digital pressure rapidly controls the bleeding. Only one haematoma of any size was precipitated: during biopsy of an external iliac gland, the haematoma resulted from damage to the pampiniform plexus of veins, but resolution occurred without infection or need to aspirate or expose the haematoma.

Although no pathological fracture of bone has followed trephine biopsy in the present series, the weakening of bone strength which must occur, requires recognition and the patient warned accordingly.

In most cases of splenomegaly much more valuable information is obtained by examination of blood, bone marrow and lymph nodes, which largely invalidates the undertaking of splenic puncture.

One death has occurred in the present series.

Case 4

P.N., male, aged 68 years, was first seen on 25th May, 1949, with multiple enlarged lymph nodes of slow development in the inguinal, external iliac and supraclavicular regions, together with splenic enlargement. A lymph node biopsy was reported by the pathologist as showing "an atypical reticulosis.

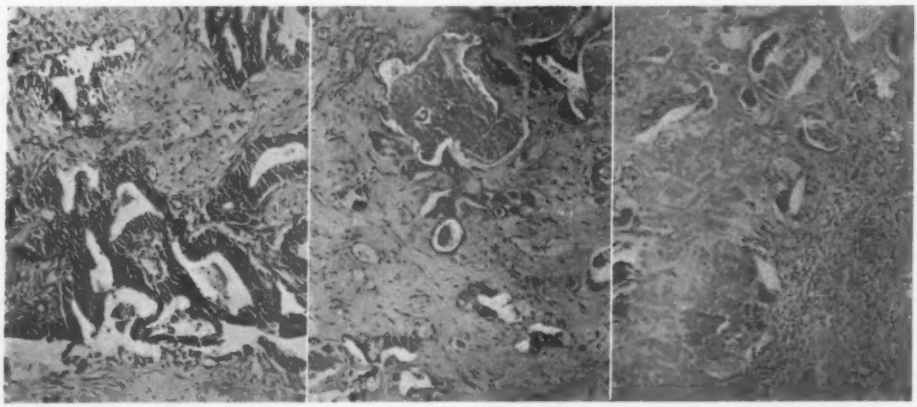

FIG. IIIa. Photomicrograph (x 150) of a liver metastasis from carcinoma of the stomach, obtained by trephine biopsy prior to commencement of deep X-ray therapy.

FIG. IIIb. Photomicrograph (x 150) of the same liver metastasis as shown in Fig. IIIa but after deep X-ray therapy, a tumour dose of 1,200 rontgens having been delivered in three weeks. Trephine biopsy specimen.

FIG. IIIc. Photomicrograph (x 150) of the same liver metastasis as shown in Figs. IIIa and IIIb, a tumour dose of 2,100 rontgens deep X-ray therapy having been given in five weeks. Trephine biopsy specimen.

In the case of liver biopsy, the rotating trephine provides a beautiful specimen and has even been used to study the effects of radiation on liver tumours (see Figs. IIIa, IIIb, IIIc). A preliminary straight radiograph of the subdiaphragmatic region to allow visualization of bowel shadows is a wise precaution in biopsy of livers which are not unduly enlarged.

In the present series the writer has had no experience of trephine biopsy of the spleen, owing to the rarity with which such information is necessary in treatment. It is felt, however, that this organ should be treated with respect and that a trephine hole may occasion severe intra-abdominal haemorrhage.

Diffuse fibrosis and foreign body giant cells are present . . . . general appearance suggests this may be a chronic form of tuberculosis."

A chest radiograph and an examination of sternal marrow were reported as normal.

Low dosage X-ray therapy was given to the lymph node areas (tumour dose 1,200r in three weeks), mediastinum (bridge technique, 1,450r tumour dose in nineteen days) and abdomen (bridge technique 700r tumour dose).

There was a complete clinical resolution of the abnormal lymphoid tissues and the patient remained well for two and a half years.

However, on 19th December, 1952, he attended with dyspnoea and asthma, and there was a right apical consolidation in the lungs determined on clinical examination. A radiograph showed a "chronic infiltrative parenchymatous lesion in the

base of the right upper lobe. No cavitation present and the mediastinum is regular and clear." Sputum tests were performed and examination and culture failed to reveal the presence of *Mycobacterium Tuberculosis*. Over the next seven months his dyspnoea progressed and became gross and general deterioration in condition took place.

It was decided that a lung biopsy was essential for diagnosis, and on 8th July, 1953, a "drill" biopsy was performed. However, owing to radiographs being unavailable, the trephine was inserted into an area of clinical dullness. A few hours later his condition deteriorated rapidly and death took place, although the presence of a tension pneumothorax was recognised and treated. The biopsy specimen consisted of normal lung tissue.

A post-mortem examination revealed the presence of a carcinoma of the lung, pulmonary embolism and pneumothorax.

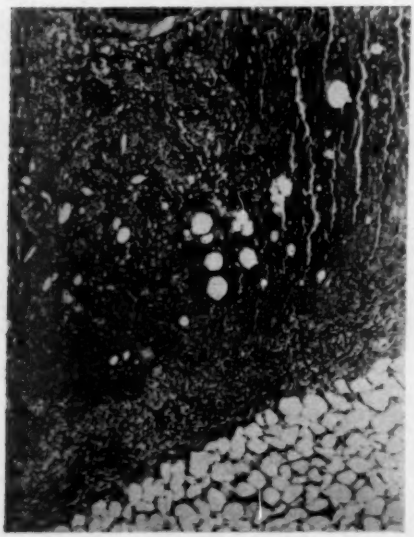

FIG. IVa. Photomicrograph (x 55) of the edge of a trephine passage in fat, filled with blood clot, and showing fibroblast in growth at the edges (preparation fifteen days following a trephine biopsy of a breast).

Tension pneumothorax following trephine biopsy of the lung is a distinct danger and has been encountered elsewhere as a lethal complication (F. Ellis, 1947). In the case recorded, an anticipation of the condition and prompt treatment may have resulted in recovery. Also radiographs should have been to hand to localize the tumour, instead of relying on percussion. However, it is the writer's considered opinion, that, allowing for a certain risk, drill biopsy is still justified in establishing diagnosis of obscure pulmonary conditions as in Case 4 in which other investigations are equivocal, to enable the institution of treatment, particularly in the case of bilateral and often inoperable disease. It is to be condemned, however, when bronchoscopic examination will provide a histological diagnosis, and in localized disease, where an exploratory thoracotomy may result in both diagnosis and surgical relief.

When trephine biopsy is to be followed by surgery aimed at a curative result, the trephine track should be placed to enable its excision in continuity with the tumour or organ. Dr. R. Motteram has demonstrated growth of tumour along a trephine track (Figs. IVa, IVb) in one case in this series which came to surgery subsequently. However, where biopsy is followed by pre-operative X-ray therapy, the precaution in placing the needle track is unnecessary. It is envisaged that pre-operative trephine biopsy

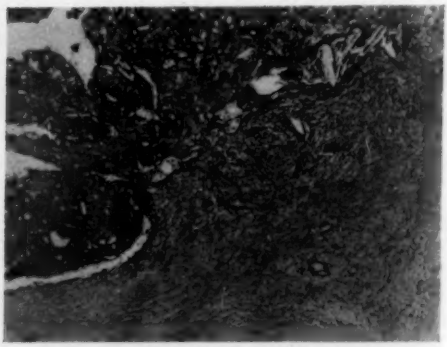

FIG IVb. Photomicrograph (x 55) showing growth of a carcinoma along the trephine passage (7 days after the biopsy).

for carcinoma of the breast may replace frozen section at the time of operation. Whether a critical interval between the times of biopsy and institution of treatment, exists in relation to prognosis (Nohrman, 1949), requires further elucidation in cancer of the breast, but would seem unlikely from experimental evidence (Maun and Dunning, 1946) and experience of behaviour of neoplasms in other sites.

ADVANTAGES OF TREPHINE BIOPSY

In the writer's experience, trephine biopsy affords the following advantages:—

(i) The procedure is rapid, causes a minimum of discomfort to the patient and is free of hazard in the majority of tumour sites. The technique is easily mastered, but requires of the operator a knowledge of anatomy (particularly surface anatomy), some adeptness in closed needling techniques, and above all, a lack of unwarranted timidity.

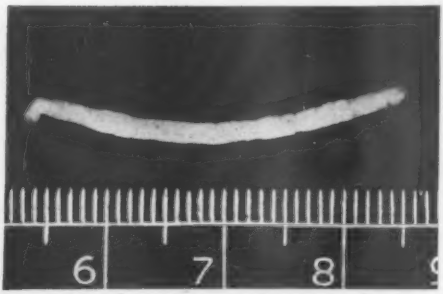

FIG. V. Photograph of the tissue core obtained by trephine biopsy from a carcinoma of the breast.

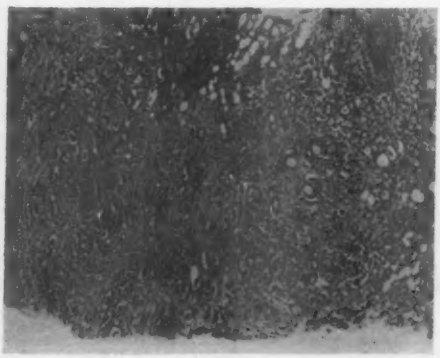

FIG. VI. Photomicrograph (x 50) showing mucoid adenocarcinoma of the breast. Trephine biopsy specimen.

(ii) The pathologist is provided with a specimen completely adequate in size (Fig. V) and is undistorted and representative of the architecture of the tumour or organ in question. The specimen lends itself completely to formal fixation, embedding, sectioning and staining (Figs. VI, VII, VIII, IX).

FIG. VII. Photomicrograph (x 50) showing primary carcinoma of the lung. Trephine biopsy specimen.

(iii) The procedure is highly reliable (93 per cent. of positive useful diagnoses in the present series), thus paralleling Kaae's results (1948) for tumours of the breast; he recorded a 92 per cent. positive useful result for trephine biopsy in non-ulcerating cases.

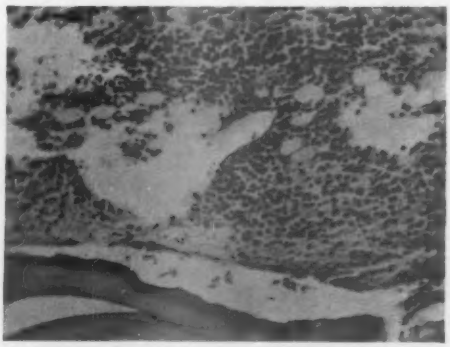

FIG. VIII. Photomicrograph (x 170) of a trephine biopsy core from the iliac crest in a case of multiple myelomatosis.

(iv) In the case of failure to obtain an adequate or representative specimen through faulty technique or difficult situation, the procedure may be repeated at will.

(v) It lends itself admirably to serial biopsy in patients undergoing radiation or chemotherapeutic treatments (Figs. IIIa, IIIb, IIIc, Xa, Xb).

(vi) Radiation treatments may be started immediately following trephine biopsy.

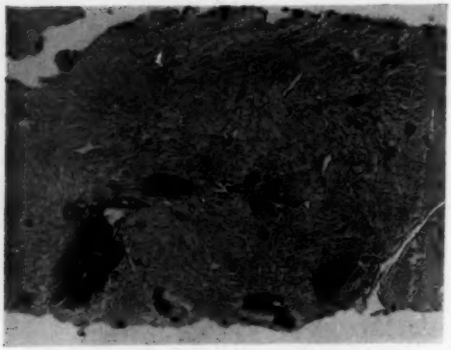

FIG. IX. Photomicrograph (x 55) of a trephine biopsy core from a primary tumour of the maxilla (fibroma with calcified foci).

(vii) There is a minimal interference with the blood supply of the tumour and clinical setting of the disease. The possible adverse effects of intrinsic tumour pressure on metastatic manifestations are reduced to a minimum.

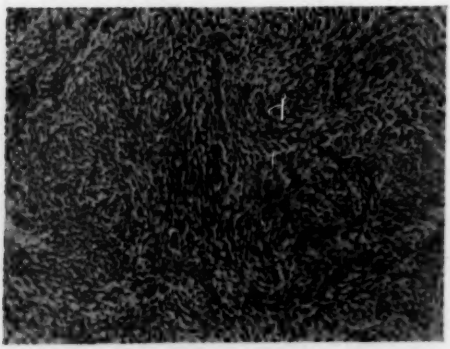

FIG Xa. Photomicrograph (x 150) of a sarcoma of the sternum prior to irradiation (trephine biopsy specimen).

(viii) In lymphadenopathies, the core is representative of the main tumour mass, and therefore establishes a diagnosis which is often missed by excision of a satellite node.

Case 5

V.M., female patient aged 33 years. Was first seen on 27th March, 1953. Two months previous a laparotomy was performed for an abdominal tumour and a "hard nodular mass 4 inches by 5 inches was found in the mesentery of the jejunum — glands along the aorta enlarged and hard."

A node was removed for examination and the pathologist reported: "Small follicles and some increase in lymphocytes. Dilated sinuses containing lymphocytes and macrophages. Non-specific chronic inflammation." (Fig. XIa.)

The patient, shortly afterwards, developed an enlarged mass of lymph nodes in the neck. A trephine biopsy was performed from the centre of the mass and showed "a complete absence of normal architecture—diffuse mass of small lymphocytes with some lymphoblasts. Lymphosarcoma." (Fig. XIb.)

It may be added that since trephine biopsy has been instituted in the Peter MacCallum Clinic, not a single excision of a lymph node for biopsy purposes has been performed, thus confirming Christiansen's experiences (1943).

(ix) Trephine biopsy is safe in heavily irradiated areas where recurrence is suspected but often unconfirmed. On the contrary, open incision of such an area is disastrous. However, even with trephine biopsy, it is wise to take the precaution of traversing relatively normal skin where this can be accomplished; otherwise the stab incision is made as small as possible and a subsequent suture is omitted.

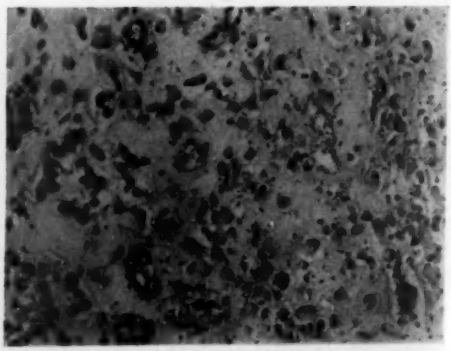

FIG. Xb. Photomicrograph (x 150) of the same tumour as illustrated in Fig. Xa, but following deep X-ray therapy (tumour dose 4,500 rontgens delivered in ten weeks). Trephine biopsy specimen.

(x) Trephine biopsy largely provides the radiotherapist with a long felt need—histological diagnosis—and and puts him on the same footing as the surgeon in assessing the results of treatment.

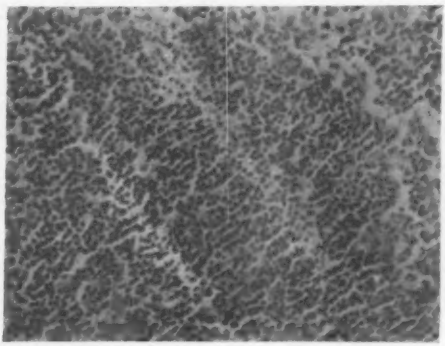

FIG. XIa. Photomicrograph (x 300) of a peripheral enlarged lymph node removed from Case 5 by formal dissection. The histological appearances are those of a chronic inflammatory change.

CONCLUSION

It may be concluded that trephine biopsy for most sites is an economic, trivial procedure which is almost compatible with office practice, and provides a biopsy specimen representative and completely adequate for formal pathological examination by means of fixation, paraffin embedding and sectioning. Furthermore, the reliability of the procedure is substantiated and should provide a positive result in over 90 per cent. of cases, once the technique has been mastered.

SUMMARY

1. Biopsy, using a high-speed rotating trephine is described and the experience of an initial 300 consecutive cases recorded and results tabulated.

2. The dangers, complications, contra-indications and advantages of the method are discussed and correlated with those of biopsy in general.

3. A high degree of reliability is recorded, with positive useful results in 93 per cent. of cases.

ACKNOWLEDGEMENTS

My thanks are due to Dr. R. Motteram, Pathologist, Cancer Institute Board, Melbourne, for his constant encouragement; to Mr. E. A. Matthaei, of the Faculty Workshop, University of Melbourne, for the photomicrographs illustrating this article, and to Mr. R. Inglis, Clinical Photographer, Royal Melbourne Hospital, for the photogaphs of the trephine apparatus and the tissue core (Figs. I, II and V).

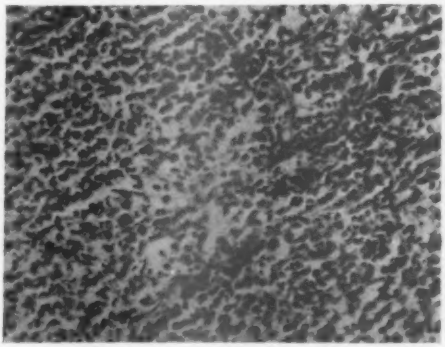

FIG. XIb. Photomicrograph (x 300) of a trephine biopsy core obtained from the centre of a mass of enlarged lymph nodes in Case 5, shownig typical lymphosarcoma. (Compare with Fig. XIa taken from the same case.)

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GUMMA OF THE LUNG

By PATRICK F. HOWDEN

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TERTIARY syphilis of the lung is now considered a rare disease. Between six to eight cases a year are reported in the literature. This apparently was not so in earlier days for as late as 1927, Tylecote estimated that the incidence of acquired pulmonary syphilis receiving sanatorium treatment for a supposed tuberculous lesion, as 1 per cent.

This case is presented since this disease is rare and the diagnosis was in doubt until the pathologist's examination and serological reports were available. A similar case has lately been reported where a pneumonectomy was performed before the Wassermann and Kahn serological reactions were obtained (Morgan, Lloyd, Price Thomas, 1952).

CASE HISTORY

A man aged 57 years who worked as a clerk, was admitted to Green Lane Hospital on 23rd June, 1953. Two months previously he had been X-rayed at his work by mass radiography and an opacity was seen in his right lung. Eighteen months previously he had an X-ray of his chest and his lung fields were then normal.

His blood picture was within normal limits. Culture of sputum revealed a moderate growth of *M. catarrhalis, streptococcus viridans* and a haemolytic streptococcus. Several sputa were found to be negative for neoplastic cells and tubercle bacilli.

Radiologist's report

10th April, 1953. *Chest* (Fig. I).—Some ill-defined opacity is seen in right lower zone with a slight suggestion of cavitation. Lung abscess is probable, but underlying neoplasm would have to be considered and progress films are advisable. The markings in the left lower zone are increased with some honey-combing rather suggestive of bronchiectasis. Linear shadows are probably pleural.

1st May. *Chest* (Fig. II).—Since 10th April the lesion in the apical and posterior basal sigments of the right lower lobe have altered somewhat in distribution without clear evidence of either extension or resolution. There is now however a well-defined circular opacity two centimetres in diameter in the upper part of the affected area. This was not previously identifiable and must be regarded as suggestive of neoplasm. Expiration film shows no evidence of bronchial obstruction, but movement of the left diaphragm is diminished by previous pleurisy.

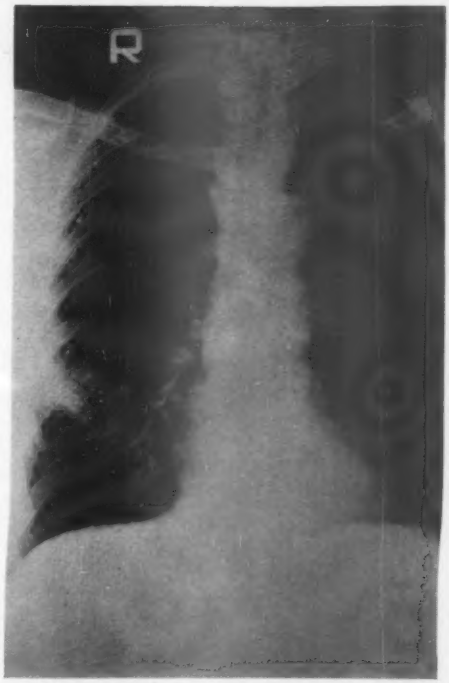

FIG. I. Radiograph of chest showing an ill-defined opacity in the right lower zone.

10th June. *Chest* (Fig. III).—There is now a small irregular cavity within the consolidation which seems to be in the subapical segment of the right lower lobe. The consolidation is more clearly defined than previously and the abscess seems to have thick walls. There is evidence of diminution in volume of the lower lobe and the presence of an underlying neoplasm cannot be excluded.

On 29th June bronchoscopy was performed and the bronchial tree was normal. The bronchial washings were negative for neoplastic cells and tubercle bacilli.

He was considered by the Consultation Committee on 29th June, and it was decided that thoracotomy was advisable since this lesion might be malignant.

Operation

On 1st July a right lower lobectomy was performed. On opening the pleura, adhesions were found over the lower lobe extending to the diaphragm and chest wall. There was an irregular "thickening" felt in the subapical area extending up into the apical segment and down into the posterior basal segment. This indurated area felt less hard than a carcinoma and was thought at the time to be chronic inflammatory in nature. The only palpable glands that could be felt round the hilum were soft and anthracotic, suggestive neither of carcinoma nor tuberculosis. The patient made an uneventful recovery from the operation.

The day following the operation Wassermann and Kahn serological tests were performed and were reported as being weak positives.

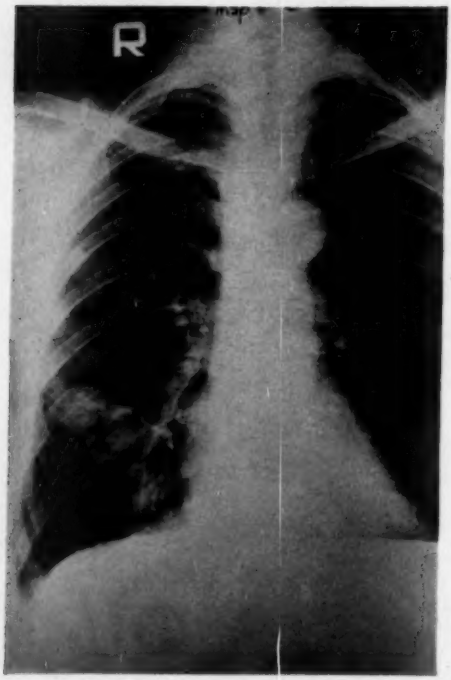

FIG. II. A well-defined circular opacity is now present in the upper part of the affected area.

After the pathological and Wassermann reaction reports the patient was further questioned and he admitted having had treatment for syphilis in 1937. At that time lumps appeared on the chin which formed ulcers and would not heal. He was seen by a skin specialist and was diagnosed as tertiary syphilis, his Wassermann reaction being positive. Injections of arsenic and bismuth were commenced and continued for several courses over an eighteen months period. His Wassermann reaction was negative at the completion of his treatment. Unfortunately he did not report for further follow-up Wassermann tests. He denied any possibility of venereal disease in his youth. In hospital penicillin injections were commenced and he was under treatment by the syphilologist on discharge from hospital on 19th July.

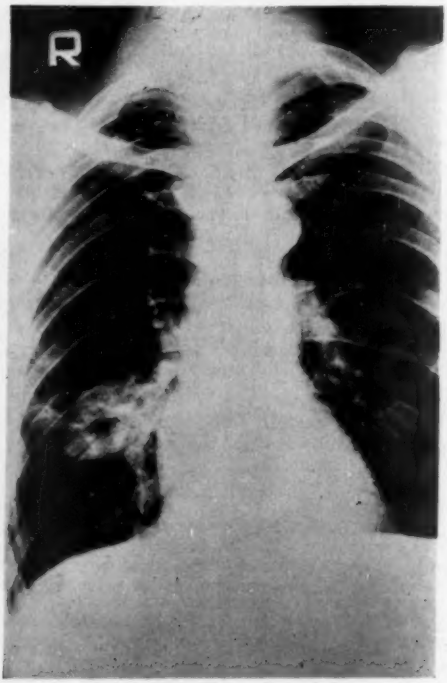

FIG. III. The apparent cavity in the consolidated area.

Pathologist's report

The pathologist first thought the lesion could be an atypical tuberculosis, but when the serological reports were at hand, he reviewed the slides and gave his full report.

The specimen (Fig. IV) is a right lower lobe showing a moderate bronchiectasis and scattered areas of caseation variable in size in the peripheral portions. The larger areas were irregular in outline and appeared to be due to coalescence of several smaller rounded areas. The centre of the nodular areas was yellowish in colour with a surrounding fibrous capsule. The visceral pleura was thickened with subpleural infiltration of the disease process.

Histology

Eight blocks from separate areas were examined. In five of these typical gummata were seen consisting of irregular shaped areas of caseous necrosis (Fig. V) in many of which indistinct outlines of

blood vessels and pulmonary alveoli can still be seen. Fragmented nuclear remnants are also present in these areas. It is evident from the variable structures of the gummata and the density of the surrounding fibrotic reaction that there is a considerable difference in the age of the lesions, some being of apparently recent origin. In other parts of the lobe there is an irregular fibrosis with areas of lymphocytic and plasma cell infiltration. The medium-sized blood vessels show a striking endarteritis and perivascular fibrosis which is most clearly seen near to the gummata (Fig. VI). Although giant cells (Fig. VII) are not common they are found in the edges of some necrotic areas, and one small focus is indistinguishable from a tuberculous lesion. Five sections stained by Ziehl-Nielson method failed to show acid fast bacilli. An unsuccessful search was made for spirochaetes in sections stained by the Warthin staining technique.

FIG. IV. The lower lobe showing the gummata and thickened pleura.

Although the first impression of these lesions was that of a fibrocaseous tuberculosis, a careful appraisal of the unusual type of necrosis, the endarteritis and the infrequency of typical giant epithelioid cells, points to tertiary syphilis.

TERTIARY SYPHILIS OF THE LUNG

DISCUSSION

The reticence of the patient concerning his previous gummatous lesions of the chin made the diagnosis difficult. Admittedly the failure to perform the Kahn and Wassermann tests was remiss on our part and might have saved this patient from a lobectomy had they been performed.

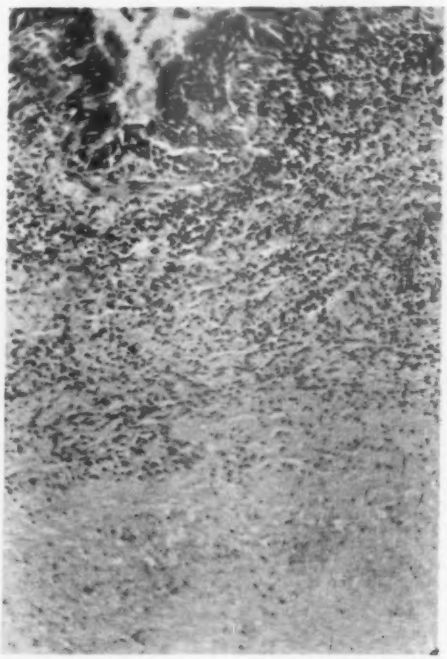

FIG. V. Showing a typical area of caseation. (x 100)

The diagnosis therefore rested on radiological findings. The X-ray film taken in February, 1953, was not available, but this was reported as being normal. The patchy irregular area of pneumonitis in the right lower lobe varied in extent over two months and in the last film, taken on 10th June a definite circumscribed opacity with an apparent cavity was present in the subapical segment of the lower lobe.

Excluding syphilis, the differential diagnosis was between tuberculosis, neoplasm and pneumonitis with abscess formation.

The negative sputa tests for tubercle bacilli and the position of the lesion seemed to rule out tuberculosis. Neoplasm was very much to the fore; but the bronchoscopic examination was normal and no malignant cells were found in several specimens of examined

sputum. This left pneumonitis with abscess formation although the good general condition of the patient and his apyrexia were against this diagnosis.

FIG. VI. Endarteritis of medium-sized vessels. (x 100)

The diagnosis of syphilis of lung was made on the serological reaction and microscopic examination of the gross specimen. On reviewing the X-ray films the lesion is seen to fit the description of a pulmonary gumma. There is the interstitial fibrosis radiating out to the periphery from the hilum with associated subpleural thickening and varying sized opacities with areas of rarefaction simulating patchy pneumonitis. Robinson (1935) recognizes three main types of lesion on X-ray.

1. *Interstitial fibrosis* radiating out from the hilum in a fan shape. The fibrosis is often bilateral and the lesion may be confused with metastatic carcinoma.

2. *Gumma of the lung* which may be miliary and multiple or solitary and discrete masses. The discrete masses appear usually near the hilum and are nodular. They may be necrosed which is demonstrated by an area of rarefaction in the central position of the nodule. Instead of necrosis, fibrosis may occur.

3. *The diffuse lobar* form is due to a bronchial lesion causing a secondary massive atelectasis resulting from a bronchostenosis.

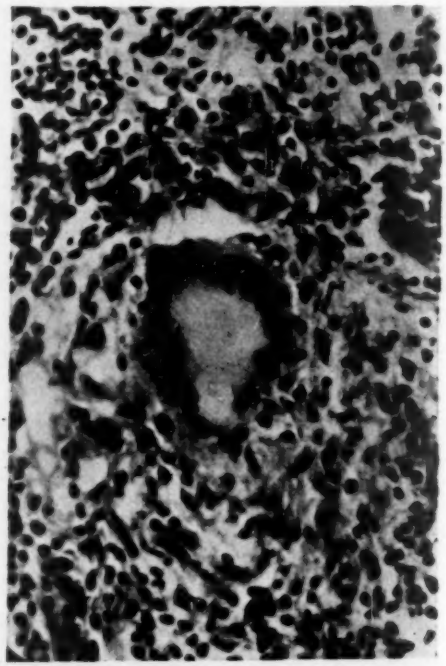

FIG. VII. Epithelioid cell nodule and a giant cell. (x 200)

Had the serological test been performed the diagnosis would probably have been made prior to operation by a trial of antisyphilitic treatment. Most gummatous lesions of the nodular type are said to resolve slowly under this treatment.

O'Leary and Ockuly (1945) recommended injections of bismuth and mapharsen at 5 daily intervals with potassium iodide three times daily as a therapeutic test lasting for a few weeks. If there is improvement during this time on serial radiography the diagnosis is clinched and the usual courses of treatment are carried out.

Indications for surgery

Exploratory thoracotomy will have to be considered in certain circumstances and sometimes a pneumonectomy or lobectomy performed.

1. An opacity is present in the lung and is thought to be neoplastic in nature. An exploratory thoracotomy is carried out without entertaining the diagnosis of gumma, no serological tests being made.

2. A known syphilitic patient with an opacity in the lung which does not resolve with treatment. Thoracotomy would be necessary to establish a differential diagnosis from malignancy. Such a case has been reported by Susman (1951), when a right lower lobectomy was performed.

3. A diffuse fibrotic lesion may affect one lung only causing a contracted fibrotic useless lung which may cause pain and dyspnoea. Pneumonectomy would rid the patient of this useless lung and cure the symptoms.

4. Where bronchiectasis is present at a late stage of the disease with its sequela of copious foul sputum and recurrent pneumonitis, resection would be of benefit in unilateral disease.

SUMMARY

A case of gumma of the lung has been described. The difficulty of diagnosing the lesion has been stressed and the differential diagnosis discussed. The indications for thoracotomy have been briefly stated.

ACKNOWLEDGEMENTS

My thanks are due to Dr. Chisholm McDowell, Physician in charge of this case, Mr. Douglas Robb, who performed the lobectomy, and Mr. Rowan Nicks for their helpful advice; Dr. Stephen Williams, the Pathologist, and Dr. John Recordon, the Radiologist, for the use of their reports; to Miss Redgwell for typing my notes, and to the Photographic Unit for their excellent photographs.

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A MECHANISM OF PRIMARY OCULOMOTOR NERVE INJURY

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OCULOMOTOR nerve lesions are recognized as being of special significance in cases of head injury. The delayed development of a fixed and dilated pupil is usually indicative of an ipsilateral space-occupying lesion, and the mechanism of its production, by pressure on the nerve by trans-tentorial herniation of the uncinate portion of the temporal lobe, is well known. But not all oculomotor nerve lesions resulting from head injury are of this type, and primary nerve injury requires differentiation.

Hooper (1951) presented twelve cases, and referred to the relevant literature. He discussed the mode of injury and the site of the lesion in the usual case. He found that the lesion usually resulted from a mid-frontal blow on the head, and that the nerve was usually involved in its course through the disrupted superior orbital fissure. Recent cases have shown an additional mechanism of injury, which is important because of likely confusion of the clinical picture with that of surface haemorrhage.

Case Notes

Four cases of head injury at the Alfred Hospital, Melbourne, presented the following relevant features:

Case 1

A man was admitted on 16th April, 1953, one and one-half hours after injury in a motor-car accident. He was semi-comatose, responding briskly to painful stimuli. There was an abrasion in the right anterior temporal region, and there were multiple fractures in the right limbs. The right pupil was widely dilated, with loss of both direct and consensual light reflexes, and the globe was central and immobile. The left pupil was of normal size and reaction to light. The head and left eye were turned to the left, and the left plantar reflex was extensor.

A right temporal burr-hole was made, and a vertical linear fracture was seen to extend into the middle cranial fossa. About 5 mls. of blood-stained fluid drained from the subdural space, and there was cortical bruising in the area of the frontal eye-field.

Consciousness was regained on the sixth day, after tracheotomy for aspiration pneumonia. The right pupil remained dilated and fixed, the globe was externally rotated, and severe ptosis was present. These abnormalities gradually improved, and on 22nd July the eye had returned almost to normal. (This patient died some months later, but autopsy was not performed.)

Case 2

A motor-cyclist who was found unconscious on the road on 18th April, 1953, was conscious but confused when admitted. There was classical "bogginess" in the right temporal fossa. Bilateral periorbital haematomata were present, the right pupil was dilated and fixed, and the globe was immobile. The left eye showed normal pupil size and reaction, and the head and left eye were turned to the left. The left plantar reflex was extensor. X-ray disclosed a right temporal stellate fracture, with extensions into the anterior and middle cranial fossae.

Operation to exclude extradural haemorrhage revealed lesions similar to those of Case 1—cortical bruising and blood-stained cerebrosphinal fluid in the subdural space. There was also a very little subdural blood clot.

Until 16th July, the right oculomotor nerve lesion remained complete, with ptosis, external rotation, and a fixed dilated pupil. His recovery was otherwise complete. By 16th January, 1954, there was great improvement, but slight ptosis, diplopia (which could be corrected voluntarily), and pupillary dilatation and sluggishness, remained.

Case 3

A young man was sent for opinion on 2nd July, 1953, with the history that fourteen days previously he had been thrown from his motor-cycle, and had remained unconscious for three days with a fixed dilated right pupil. He had then regained consciousness, and the pupil had become of normal size and reaction. Two days later, the right pupil had again become dilated and fixed, but he had remained fully conscious and alert.

Examination discovered a complete right oculomotor nerve lesion as the only abnormality. X-ray showed a linear fracture running down to the middle cranial fossa from the right mid-temporal region. The calcified pineal gland was in the midline.

This patient has not been seen recently, but it is reported that there has been some return of power in the levator palpebrae superioris, and in the internal rectus muscle. Serious diplopia persists and the pupil remains widely dilated.

Case 4

A woman was a front-seat passenger in a motor-car when, as the result of a collision, her head struck and dented the near-side windscreen pillar. She then spoke to her husband, but soon lost consciousness. On admission to hospital she was deeply semi-comatose. There was an abrasion in the left temporal region. The right arm and leg were held spastically in flexion, and the right plantar reflex was extensor. The pupils were equal, and reacted briskly to light. The head and right eye were turned fixedly to the right, whilst the left eye was central with a medial rectus palsy. X-ray of the skull showed a vertical left temporal fissure fracture.

Over the next thirty-six hours, her condition gradually became worse, left hemiplegia developed, and she assumed the posture of decerebrate rigidity, in full coma. Bilateral temporal burr-holes revealed no abnormality other than slight subarachnoid haemorrhage, and ventriculography confirmed the absence of any space-occupying lesion. She did not recover full consciousness for six weeks, during which tracheotomy was necessary to secure a safe airway.

After six months, she is fully alert mentally, speaks fairly well, but has a spastic left hemiparesis, and gross ataxia of the right arm and leg. She still suffers some diplopia, and there is weakness of the left levator palpebrae superioris and internal rectus muscles.

Case Commentary

These four patients suffered a similar pattern of injury — a blow in the anterior temporal region resulting in a temporal fracture. In three there was a complete third nerve lesion, while in Case 4 the oculomotor lesion was only partial. In three cases there was clinical and surgical evidence of cerebral contusion in the region of the frontal eye-field.

Each case simulated to some extent the clinical picture of cerebral compression. In Case 1, a temporal injury, an ipsilateral fixed dilated pupil, a contralateral hemiplegia, and a suggestion of increasing unconsciousness, were the reasons for surgical exploration. In Case 2, similar findings in a conscious patient were accepted as indication for surgery, although the similarity to Case 1 suggested the diagnosis of primary oculomotor nerve injury. Operation was undertaken with the knowledge that extradural haemorrhage is best treated before consciousness is lost. Case 3 was seen so late that the diagnosis was not then in doubt, and surgical intervention was obviously not required. Earlier in the clinical course, the possibility of compression must have caused anxiety. Case 4 presented the picture of a primary brainstem haemorrhage, and exploration was undertaken only as a "last-chance" measure when deterioration occurred.

In Cases 1, 2 and 3, the oculomotor nerve lesion occurred as a relatively isolated event, and in the first two of these it recovered sufficiently for useful function — in Case 2 after an interval of three months. In Case 3, the pupil is said to have recovered its normal size and activity for two days shortly after injury, but then to have again become dilated and fixed. The reason for this behaviour is not known. Case 4, in which the nerve lesion was only partial and did not affect pupil size and activity, still shows obvious signs of a brainstem lesion, but the nerve is recovering.

Discussion

The differential diagnosis of primary oculomotor nerve injury must include the Hutchinsonian pupil of cerebral compression. The main distinguishing feature of compression is the special march of events—constriction, followed by dilation — at an interval after injury. But this early stage may not be observed. The main abnormality is of the pupil, the external ocular musculature being relatively little affected at first. Subsequent similar changes in the contralateral pupil, together with disturbances of consciousness, circulation, and respiration, complete the picture. By contrast, the primary third nerve lesion is usually maximal from the beginning, and the external ocular musculature is as much involved as the internal.

There are two obvious sites at which the nerve may be damaged. The first is at the superior orbital fissure, and of Hooper's twelve cases (supra), all but one resulted from a mid-frontal impact causing disruption of that fissure, in which the nerve was contused or lacerated. The second site is within the brainstem, and Hooper's other case, like the present Case 4, showed clear signs of a brainstem lesion.

Cases 1, 2 and 3 suffered a quite different mode of injury—a retarding impact in the anterior temporal region. In none of these was the superior orbital fissure involved in a fracture line, and none sustained brainstem damage. The most likely mechanism of nerve involvement in these cases is stretch injury

in continuity, resulting from cerebral rotation or displacement, due to the impact. The nerve behaves as a peripheral nerve, and recovery, of greater or less degree and after a variable time interval, is to be expected as long as the nerve has not been severed. In Case 4 a similar traction upon the nerve may have caused the brainstem haemorrhage.

The importance of this mechanism of injury rests in the fact that the coincidence of temporal trauma with a fracture line crossing the middle meningeal vessels makes confusion with extradural haemorrhage likely. When doubt exists, craniotomy must be undertaken, for it should not harm these patients, but delay in the case of extradural haematoma may be fatal.

Finally, several cases of extradural and subdural haemorrhage have been remarkable for the slowness of recovery of their secondary oculomotor nerve lesions, and have shown an interesting disproportion in their oculomotor signs. Sunderland and Hughes (1946) showed that the pupillo-constrictor fibres occupy chiefly the superior surface of the oculomotor nerve in the tentorial gap. Uncinate herniation should therefore affect these fibres first and predominantly, but in some cases the external ocular paralysis is seen to be relatively gross while the pupil is still reacting to light. This suggests that in these cases the Hutchinsonian effect may be superimposed upon a primary injury to the nerve.

SUMMARY

Four cases of primary oculomotor nerve lesion in head injury are presented, and the diagnostic features are described.

The mode of injury — a blow in the anterior temporal region without damage to the superior orbital fissure—is different from that previously described.

The mechanism of nerve damage—stretch injury in continuity—and its significance are discussed.

This lesion is particularly liable to confusion with extradural haemorrhage.

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Books Reviewed.

CLINICAL CHEMISTRY IN PRACTICAL MEDICINE.

By C. P. STEWART, D.Sc., Ph.D., and DUNLOP, D.M., B.A., M.D., F.R.C.P.(Edin.), F.R.C.P.(Lond.). Fourth Edition. Edinburgh: E and S Livingstone Ltd., 1954. 8½" x 5½", vii plus 320 pp, 27 figures. Price: 21s. net.

This is the fourth edition of what has been, for students, a valuable adjunct in the field of applied biochemistry. The position is very different now from what it was when the first edition was published and the authors' statement that "biochemistry is in danger of being over emphasized in medicine to the detriment of careful history taking and bedside examination of patient" is rather an understatement of the present situation. Because of its extraordinary growth it is necessary to remember that this is merely one of the many techniques that are used by the practitioner. On the other hand it is a very important one and one of which he must be fully cognizant and, indeed, possess considerable knowledge.

The present volume is of particular value in that it keeps a nice balance between the various methods of examination and their application to the special problems. Of particular interest is the section on "The Significance of the Normal" in the introductory chapter.

In all parts the general problem is discussed and physiology and clinical features receive their deserved attention. Perhaps the only criticism that might be levelled is that the standard of pathological information is not high.

The volume covers a large field from water and electrolyte metabolism, through the disturbances and functions of very many systems in the body, to general hormone and nutritional changes.

There are appendices dealing with actual methods of examination which will be particularly valuable to the young student and there are discussions of the normal composition of urine and blood.

Altogether this is a particularly valuable book for the student and, indeed, for the busy practitioner who may wish to check or augment his knowledge rapidly and easily on the more or less current routine problems of this kind.

The general presentation of the material is clear and there is a satisfactory index.

SURGERY FOR DENTAL STUDENTS.

By MICHAEL F. A. WOODRUFF, M.D., M.S.(Melb.), F.R.C.S.(Eng.). England: Blackwell Scientific Publications, 1952. 8½" x 5½", viii plus 326 pp., 108 illustrations. Price: 30s.

Dental science has now reached a stage when it not only deserves, but demands, appropriate provision for the teaching of the future members of the dental profession. In the past many medical textbooks were "made to do" for dental students, and appropriate chapters were prescribed to supplement systematic lectures in the dental course. The inevitable result was that frequently the dental student was not adequately taught the fundamentals of basic subjects such as general medicine and general surgery. In recent years there have been a few genuine attempts by British authors to write textbooks on basic subjects specifically designed for teaching dental students. None has been more generally successful than the volume by Professor Woodruff under review.

Surgical principles, relevant to applied anatomy, and related clinical pathology are well integrated throughout the book. Photographic and X-ray illustrations are adequately clear and demonstrative; some diagrams, however, could be improved.

The main constructive criticisms which can be offered are generally related to clinical dental surgery, and it is a matter for regret that in a textbook designed for dental students there are so many dental lapses. For example, the representation of teeth in Figures 36 and 39 are sufficiently bad as to make a dental student almost lose confidence in the correctness of other anatomical diagrams. On page 124, the relationship of teeth to the antrum is not accurately or adequately described. On page 11, in the description of the examination of the mouth, no mention is made of the use of a cheek or lip retractor, without which it is impossible to examine most mouths adequately.

On page 12, the statement is made "in serious cases, make a thorough examination of the cardiovascular and respiratory systems, the abdomen, and the nervous system." This may lead to misunderstanding among students because dental surgeons do not pretend to be qualified to make such an examination. In a serious case the responsibility would be handed to the specialist anaesthetist. On page 20, the words "local anaesthetics" are used instead of "local analgesics."

On page 22, "a carious tooth" would better be described as "a badly carious tooth."

On page 25, it is pointed out that the sterilization of a cavity like the mouth is impossible, but there is no mention of the benefit of immediat preoperative cleaning of the mouth and teeth with one of the modern detergent solutions. Such a technique removes sordes and mucus, and does undoubtedly temporarily decrease the oral bacterial flora.

On page 100, primary, reactionary, and secondary haemorrhage appear to be related only to arterial haemorrhage — a student could get the erroneous impression that the bleeding from venous vessels is not so classified. On page 101, the small paragraph entitled "Haemorrhage following Extraction" is sketchy, and either should be adequately amplified or omitted in a textbook for dental students.

The section on Vincent's angina rather confuses the different clinical pictures seen on the tonsil and in the gingival tissues. It is not clearly indicated

that the technique of treatment in these two situations can differ; i.e. it is useless to give Intra-venous Therapy for purely interdental alveolar infections because the lesions are extra-vascular.

To state that the term "epulis" is applied to only two types of this tumour is an over-simplification of classification (page 184). Also, exception must be taken to the statement that the giant cell epulis is less common than the fibrous epulis.

The general principles of treatment of fractures are very well set out, but a number of the dental references to this subject are open to criticism. For example, few people would agree that interdental wiring in the treatment of jaw fractures is "not an ideal method of fixation"; because where this method is applicable, it is one of the really ideal forms of treatment.

While both the author and publishers may be offered congratulations on this volume, it is to be hoped that in the second edition (and it is confidently expected that there will be one) a closer liaison with current dental clinical practice and a wider appreciation of oral pathology will be apparent.

RECENT ADVANCES IN SURGERY.

By H. EDWARDS, M.S., C.B.E., F.R.C.S., with Forword by Sir HENEAGE OGILVIE, K.B.E. Fourth Edition. England: J. and A. Churchill Limited, 1954. 8" x 5¼", xiv plus 480 pp., 157 illustrations. 40s. net.

In this age when the march of surgery has been so rapid and its advances so prodigious, there has been a mass of surgical novelty introduced and at the same time even a departure from established surgical precedent. It might therefore be questioned whether such a book as Mr. Edwards has produced could maintain a sense of balance and proportion, having regard to the surgical subjects which his work embraces. It is apparent that he has given some thought to this matter, for it is noticeable that his collaborators exceed in number, those who contributed to the previous edition of this excellent book. In his wisdom the Editor has called upon his surgical friends who are recognized as masters of their specialty in Great Britain. We suggest that this action has resulted perhaps in a more exact sifting of the surgical wheat from the chaff than formerly, and this purpose has been achieved without detracting from the individual nature of the book and without disturbing its balance as a whole.

It would be presumptuous to criticize any particular section of the book for each part has been compounded by men who have at their finger tips, the subject about which they write. It may be that some of the opinions which are given will be found at some future time, to be inexact. It will be the function of later editions of this work to correct these errors in the light of more recent advances in surgery.

But surely for the present this book provides a very considered opinion from those men, whose experience and reputation entitles them to inform their readers of the current practice of British surgery at its best.

We congratulate the Editor, Mr. Edwards and his associates. The book will surely have a wide appeal and to the young post graduate seeking higher surgical qualifications it should prove indispensable. The present edition of "Recent Advances in Surgery" we assess as the surgical book of the year.

SURGICAL UROLOGY.

By R. H. FLOCKS, M.D., and DAVID CULP, M.D. Chicago, U.S.A.: Year Book Publishers Inc., 1954. 8¼" x 5¾", ix plus 392 pp., 118 illustrations. Price: $9.75.

The authors have produced a very useful handbook of operative urology.

It will be found particularly useful by house-surgeons and post-graduate surgical students and also, on occasions, to the practicing urologists and teachers of urology. There are sections devoted to the kidney, ureter, bladder, prostate, urethra and genitalia, and these sections include descriptions of all the commonly performed surgical procedures, with a short section on anatomy and physiology.

The descriptions of the operations are short and concise and do not go into detail but are quite adequate for the guidance of any one with reasonable surgical knowledge and training. Some of the minor procedures are particularly well described. For example, epididymo-vasostomy for the relief of sterility and suggested procedures for the surgical correction of urinary incontinence. Other sections, such as that on transurethral prostatic resection are necessarily brief. The authors have compressed into a small book a surprisingly large amount of information and a surprisingly complete summary of urological operations.